

RS-ULS-91-009

APRIL 1991

oreign
roadcast
information
ervice



ANNIVERSARY
1941 - 1991

JPRS Report

Science & Technology

USSR: Life Sciences

Science & Technology

USSR: Life Sciences

JPRS-UIS-91-009

CONTENTS

18 APRIL 1991

Aerospace Medicine

Hormonal Regulators of Calcium Metabolism Following Space Flights of Various Durations [L. G. Pozharskaya and V. B. Noskov; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	1
Computer Tomography Measurement of Vertebral Bones and Muscles After Extended Manned Space Flights [V. S. Oganov, K. Kann, et al.; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	1
Functional Activity of Hypophyseal-Thyroid System During 370-Day Antiorthostatic Hypokinesia [Ye. N. Kabitskiy; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	1
Changes in Rheologic Indices of Blood and Hemodynamics During 14-Day Antiorthostatic Hypokinesia [A. P. Ivanov, I. B. Goncharov, et al.; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	2
Higher Plants as Part of Biological Human Life Support System [I. Ye. Ivanova, T. A. Derendayeva, et al.; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	2
Biochemical Aspects of Human Adaptation to Combined Effect of Antiorthostasis, Decreased Barometric Pressure, and Increased Oxygen Content [T. N. Balandina, Ye. I. Nikitin, et al.; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	2

Agricultural Science

Production of Verticillin Bioinsecticide [Ye. F. Solovov; <i>ZASHCHITA RASTENIY</i> No 6, Jun 90]	4
---	---

Biochemistry

Structure of recA Gene of <i>Pseudomonas aeruginosa</i> [V. M. Kryukov, Ye. N. Zaytsev, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	6
Chemical Reactions in Double-Stranded Nucleic Acids. Part 10. Kinetics of Oligomer Ligation by Water-Soluble Carbodiimides [N. G. Dolinnaya, A. V. Tsyrovich, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	6
Chemical Reactions in Double-Stranded Nucleic Acids. Part 11. Correlation Between Kinetics of Chemical Ligation of DNA Duplexes and DNA Modification at Reaction Site [N. G. Dolinnaya, A. V. Tsyrovich, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	6
Structure of Photosynthetic Reaction Center of Green Thermophilic Bacterium <i>Chloroflexus aurantiacus</i> [M. A. Kutuzov, B. Ye. Shmukler, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	6
Synthesis and Reactivity of Novel Water-Soluble Carbodiimides [M. N. Gertsyuk, V. N. Sergeev, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	7
Peptide With Universal Tryptophanyl-tRNA Synthase Epitope [T. A. Zargarova, A. A. Zargarov, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	7
Replicative Complex of Tick-Borne Encephalitis Virus (TBEV). Part 2. Effects of Envelope Protein E (EPE) and Anti-EPE Antibody on In Vitro RNA Synthesis [O. V. Morozova, N. A. Belyavskaya, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	7
Synthesis of Histidine and Carnosine Phosphoanalogs [A. R. Khomudov; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	8
Exposure of HIV-1 gp41 Transmembrane Protein Epitopes on Surface of Hepatitis B Core Antigen Capsids [R. Ulrikh, G. P. Borisova, R. Mering, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	8
Chemical Reactions in Duplex DNA. Part 12. Novel Gene Assembly Strategy [Z. A. Shabarova, I. N. Merenkova, et al.; <i>BIOORGANICHESKAYA KHIMIYA</i> , Vol 16 No 9, Sep 90]	8

Biophysics

- Effects of Ultraviolet Light on Bacteriorhodopsin
[L. S. Broun, A. A. Kononenko, et al.; *RADIOBIOLOGIYA* Vol 30 No 4, Jul-Aug 90] 9

Biotechnology

- Preclinical Trials With Soviet Recombinant Human Interferon- A2 (Reaferon)
[Yu. T. Kalinin, A. A. Vorobyev, et al.; *ZHURNAL MIKROBIOLOGII, EDIDEMIOLOGII I IMMUNOBIOLOGII* No 6, Jun 90] 10

Epidemiology

- Increased Cholera Incidence Due to Contaminated Water [L. Dmitriyeva; *IZVESTIYA*, 23 Aug 90] 11
Catastrophic Hepatitis Situation [S. Tutorskaya; *IZVESTIYA*, 16 Aug 90] 12
Hepatitis in Uzbekistan [M. Mukhammad-Dost; *PRAVDA VOSTOKA*, 28 Jul 90] 13
Concern About AIDS in Uzbekistan [M. Mukhammad-Dost; *PRAVDA VOSTOKA*, 29 Jul 90] 15
Malignant Melanoma Incidence in Moscow
[T. S. Sitnikova, R. F. Garkavtseva, et al.; *VOPROSY ONKOLOGII*, Vol 36 No 6, Jun 90] 16
Identification of Borrelia Isolated in USSR and Czechoslovakia From Ixodes ricinus Ticks
[V. M. Kryuchevnikov, E. I. Korenberg, et al.; *ZHURNAL MIKROBIOLOGII, EDIDEMIOLOGII I IMMUNOBIOLOGII* No 6, Jun 90] 16
Ornithosis Outbreak at Textile Plant
[Yu. Ya. Vengerov, Yu. M. Fedorov, et al.; *ZHURNAL MIKROBIOLOGII, EDIDEMIOLOGII I IMMUNOBIOLOGII* No 6, Jun 90] 16
Human T-Cell Leukemia Virus Type I (HTLV-I) Antibody Screening in Sera of Adult Population in Some Regions of USSR
[N. B. Senyuta, L. S. Yakovleva, et al.; *VOPROSY VIRUSOLOGII*, Vol 35 No 4, Jul-Aug 90] 17
Plague in Aral Region [K. Imanberdiyev; *KAZAKHSTANSKAYA PRAVDA*, 18 Sep 90] 17
Outbreak of Plague in Uzbekistan 'Localized' [Unattributed Article; *PRAVDA*, 14 Nov 90] 17

Genetics

- Cytogenetic Sequelae of Wide-Band Noise
[O. I. Timchenko, Ye. N. Shantyr, et al.; *GIGIYENA TRUDA I PROFESSIONALNYE ZABOLEVANIYA* No 9, 90] 18
Effects of Elevated Ambient Temperatures on Myocardium: Clinical and Experimental Studies
[L. I. Bilyk, T. P. Kostenko, et al.; *GIGIYENA TRUDA I PROFESSIONALNYE ZABOLEVANIYA* No 9, 90] 18
All-Union Seminar of Young Scientists and Specialists on "Novel Biomolecular Aspects of Occupational Pathology, Toxicology and Hygiene"
[L. M. Komleva, V. V. Ivanov; *GIGIYENA TRUDA I PROFESSIONALNYE ZABOLEVANIYA* No 9, 90] 18

Human Factors

- Individual Stereotypes of Human Neuropsychic Prognostic Activity in Problem Situations With Different Probability Structures
[A. Krauklis, I. Kazanovskaya; *IZVESTIYA LATVIYSKOY AKADEMII NAUK*, No 9, Sep 90] 19

Immunology

- Field Trials with Plasma Subunit Hepatitis B (PSHB) Vaccine
[V. N. Ikoyev, M. A. Gorbunov, et al.; *ZHURNAL MIKROBIOLOGII, EDIDEMIOLOGII I IMMUNOBIOLOGII*, No 6, Jun 90] 26
Postinfectional and Postvaccinal Anthrax Immunity in Humans
[V. A. Abalakin, Sh. S. Dzhabirov, et al.; *ZHURNAL MIKROBIOLOGII, EDIDEMIOLOGII I IMMUNOBIOLOGII*, No 6, Jun 90] 26

Development of Acarid Antigen-Based Vaccines and Antisera for Prophylaxis of Tick-Borne Encephalitis (TBE) [V. I. Votyakov, N. P. Mishayeva; <i>ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII</i> , No 6, Jun 90]	26
Immunostimulant Properties of Ethylene Oxide and Propylene Oxide Block Copolymers (Poloxamers) [I. N. Topchuyeva, S. G. Zaygorodniy, et al.; <i>IMMUNOLOGIYA</i> , No 4, Jul-Aug 90]	26

Laser Bioeffects

Laser Treatment of Heart Arrhythmia [B. Samoylov; <i>LENINGRADSKIY PRITVET</i> , 30 Aug 90]	28
Safety Assessment of New Laser Devices [L. I. Lapkina, A. V. Levina, et al.; <i>GIGIYENA TRUDA I PROFESSIONALNOYE ZABOLEVANIYA</i> , No 6, Jun 90]	28
Maximum Permissible Level of Laser Radiation With a Wavelength of 10.6 Microns [I. N. Ushkova, N. N. Petrishchev, et al.; <i>RADIOBIOLOGIYA</i> , Vol 30 No 4, Jul-Aug 90]	28

Medicine

Management of Severe Brucellosis With Xenobiosorption [L. Ye. Tsirelson, T. A. Popov, et al.; <i>KLINICHESKAYA MEDITSINA</i> , Vol 68 No 6, Jun 90]	32
Progress in Introducing Sorption Therapy for Radiation Victims [V. G. Nikolayev Interview; <i>PRAVDA UKRAINY</i> No 420, 18 Oct 90]	32
Soviet-Vietnamese Joint Enterprises for Homosorbent Production [I. Tikhomirov; <i>PRAVDA</i> No 294, 21 Oct 90]	33
Antibiotic Therapy of Armenian Earthquake Victims With Crush Injuries [E. A. Nechayev, I. D. Kosachev, et al.; <i>ANTIBIOTIKI I KHIMIOTERAPIYA</i> , Vol 35 No 10, Oct 90]	33

Military Medicine

Device for Personal Prevention of Sexually Transmitted Diseases [V. G. Pankratov and R. N. Pilkevich; <i>ZDRAVOOKHRANENIYE BELORUSSII</i> , No 10, Oct 90]	34
Surgical Strategy in Landmine Trauma [L. N. Bisenkov, Ye. K. Gumanenko; <i>VESTNIK KHIRURGII IMENI I. I. GREKOVA</i> , Vol 145 No 10, Oct 90]	34
Hemosorption-Facilitated Healing of Severe Burns [N. Ye. Povstyanov, A. F. Fedotov, et al.; <i>VESTNIK KHIRURGII IMENI I. I. GREKOVA</i> , Vol 145 No 10, Oct 90]	34
Determination of Microbial Sensitivity to Antiseptics [V. M. Buyanov, G. V. Rodoman, et al.; <i>VESTNIK KHIRURGII IMENI I. I. GREKOVA</i> , Vol 145 No 10, Oct 90]	34

Nonionizing Radiation Effects

Protective Activity of Mexamine in Rats Following Electromagnetic Irradiation [S. A. Bugrov, B. I. Davydov, et al.; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	35
--	----

Pharmacology, Toxicology

Antiretroviral Drug Developed at Armenian Institute [Unattributed Article; <i>MOSCOW DOMESTIC SERVICE</i> , 29 Jul 90]	36
Effect of a Perfluorocarbon Emulsion—An Inducer of Enzymes of the Liver's Cytochrome P-450-Dependent Monooxygenase System—on Acute Toxicity of CCl ₄ and on the Effectiveness of Preventive Use of Antidotes in Organophosphorus Pesticide Intoxications [G. Mikhaylov, A. Varykhanov, L. Omarova, I. Terovskiy, V. Obraztsov; <i>FARMAKOLOGIYA I TOKSIKOLOGIYA</i> , Vol 53 No 4, Jul-Aug 90]	36
Psychomotor Stimulants as Performance-Enhancing Drugs [A. V. Smirnov; <i>FARMAKOLOGIYA I TOKSIKOLOGIYA</i> , Vol 53 No 4, Jul-Aug 90]	39
N-5(Hydroxynicotinoyl)-L-Glutamic Acid: Novel Substance With Nootropic Activity [T. A. Voronina, T. L. Garibova, et al.; <i>FARMAKOLOGIYA I TOKSIKOLOGIYA</i> , Vol 53 No 4, Jul-Aug 90]	44

Chronic Administration of Melatonin Attenuates Effect of Imizine on Dynamics of Forced Swimming and Circadian Rhythms of Movement in Rats [K. B. Ovanesov, V. A. Baturin, et al.; <i>FARMAKOLOGIYA I TOKSIKOLOGIYA</i> , Vol 53 No 4, Jul-Aug 90]	44
Analgesic Activity of Coordination Compounds of Methionine-Enkephalin and Bivalent Metals [L. A. Gromov and E. A. Serdyuk, <i>FARMAKOLOGIYA I TOKSIKOLOGIYA</i> , Vol 53 No 4, Jul-Aug 90]	45

Physiology

Audiogenic Reactions of Rats Following Ultraviolet Radiation of Their Eyes [G. V. Lobacheva; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	46
Superslow EEG Oscillations and Velocity Correlates of Problem Solving [G. A. Aminev, A. R. Kudashev; <i>FIZIOLOGIYA CHELOVEKA</i> , Vol 16 No 7, Jul-Aug 90]	46
Physiological Dynamics of Monotonous Operation 1.5 h in Duration [Yu. G. Grigoryev, S. N. Lukyanova, et al.; <i>FIZIOLOGIYA CHELOVEKA</i> , Vol 16 No 7, Jul-Aug 90]	46
Temporal Factors in Psychophysiological Adjustments of Information Systems Experts [A. P. Shulga, S. V. Guskov; <i>FIZIOLOGIYA CHELOVEKA</i> , Vol 16 No 7, Jul-Aug 90]	46
Determination of Informational Load in Operators [O. Yu. Netudykhatka, V. N. Yevstatyev, et al.; <i>FIZIOLOGIYA CHELOVEKA</i> , Vol 16 No 7, Jul-Aug 90]	47
Physiologically Active Substances Unattributed Article; <i>IZIOLOGICHESKI AKTHIVNYE VESHCHESTVA</i> , TOM 21, 1989	47

Public Health

Health Care System and AIDS [T. Bystrova; <i>VETERIN</i> , 6-12 Aug 90]	60
Ministry of Health Scientific Center Explains Chernobyls Illness [V. Popkov; <i>SEMYA</i> , No 32, 6-12 Aug 90]	60
Difficulties in Diagnosing AIDS in Uzbekistan [Ye. Lamikhova; <i>KOMSOMOLETS UZBEKISTANA</i> , 20 Jul 90]	61
Special Scientific Session on Perinatal Pathology and Infant Mortality Held in Tashkent [Unattributed Article; <i>VESTNIK AKADEMII MEDITSINSKIKH NAUK SSSR</i> , No 7, Jul 90]	61
Regional Features of Infant Mortality [M. Ya. Studenikin, Ye. A. Leparskiy, et al.; <i>VESTNIK AKADEMII MEDITSINSKIKH NAUK SSSR</i> , No 7, Jul 90]	62
Program for Reducing Infant Mortality in the Uzbek SSR S. Bakhrarov; <i>VESTNIK AKADEMII MEDITSINSKIKH NAUK SSSR</i> , No 7, Jul 90]	66
Causes of the Death of Children in Their First Year of Life in Rural Uzbek SSR I. R. Klibley, M. U. Nizamova, et al.; <i>VESTNIK AKADEMII MEDITSINSKIKH NAUK SSSR</i> , No 7, Jul 90]	69

Radiation Biology

Concomitant Radiation Effects, Their Immediate and Remote Consequences [Ye. Ye. Gogin; <i>TERAPEVTICHESKIY ARKHIV</i> , Vol 62 No 7, Jul 90]	72
Changes in Electrical Parameters of Rat Skin During Radiation [S. N. Katasonov, S. K. Shishkina, et al.; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	76
Physiological Aspects of Dogs' Ability to Maintain Posture During Primary Reaction to Radiation [V. N. Malakhovskiy, O. A. Stemparchetskiy, et al.; <i>KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA</i> , Vol 24 No 4, Jul-Aug 90]	76
Reciprocal Translocations in Mice in Chernobyl Area [M. D. Pomerantseva, L. K. Ramava, et al.; <i>RADIOBIOLOGIYA</i> , Vol 30 No 4, Jul-Aug 90]	77
Partial Sterility of Pine Trees in 1986 and 1987 in Chernobyl Area [L. V. Khromova, M. G. Romanovskiy, et al.; <i>RADIOBIOLOGIYA</i> , Vol 30 No 4, Jul-Aug 90]	77
Spontaneous Motor Activity and Physical Endurance in Rats With Radiation Injuries Treated With Radioprotective Agents [T. M. Mamadzhanyov; <i>RADIOBIOLOGIYA</i> , Vol 30 No 4, Jul-Aug 90]	77
Book on Blood Chemiluminescence for Estimating Radiation Damage [A. Sverdlov; <i>RADIOBIOLOGIYA</i> , Vol 30 No 4, Jul-Aug 90]	77

Virology

Radioimmunoprecipitation in Laboratory Diagnosis of AIDS: Optimization and Technical Assessment [S. Yu. Klyushnik, L. M. Selimova, et al.; <i>ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII</i> , No 6, Jun 90]	79
Enhanced Penetration of Human Immunodeficiency Virus Into Cells With Helper Virus [N. K. Sharova, A. G. Bukrinskaya; <i>VOPROSY VIRUSOLOGII</i> , Vol 35 No 4, Jul-Aug 90]	79
Cultivation and Physico-Chemical Properties of Lassa Virus, Josiah Strain [F. M. Fidarov, L. Ye. Surikova, et al.; <i>VOPROSY VIRUSOLOGII</i> , Vol 35 No 4, Jul-Aug 90]	79
Comparative Analysis of Hepatitis That is Neither A nor B With Fecal-Oral Means of Transmission in USSR and India [I. V. Shakhgildyan, M. S. Chadkha, et al.; <i>VOPROSY VIRUSOLOGII</i> , Vol 35 No 4, Jul-Aug 90]	79
Vaccinia Virus Stimulation of Oncogenesis in C57B1 Mice [N. A. Kharkovskaya, S. A. Khristalev, et al.; <i>VOPROSY VIRUSOLOGII</i> , Vol 35 No 4, Jul-Aug 90]	80
HIV-Like Particle in Subjects With Indeterminate Immunoblotting Patterns [R. M. Khaitov, G. N. Chuyirov, et al.; <i>IMMUNOLOGIYA</i> , No 4, Jul-Aug 90]	80
In Vitro Protective Action of Antisera Against Synthetic Fragment of HIV-1 gag Gene Protein p24 [A. L. Liozner, A. N. Byzina, et al.; <i>IMMUNOLOGIYA</i> , No 4, Jul-Aug 90]	80
Detection of HIV Antibodies by Agglutination of Latex Particles Coated With Synthetic Epitopes [I. G. Sidorovich, S. P. Pavlikov, et al.; <i>IMMUNOLOGIYA</i> , No 4, Jul-Aug 90]	81

Miscellaneous

Computerized Surveillance of Antimicrobial Resistance of Pyogenic Pathogens [N. A. Semina, K. K. Gladkova, et al.; <i>ANTIBIOTIKI I KHIMioterapiya</i> , Vol 35 No 10, Oct 90]	82
Cloning of aacC2 Gene From E.coli Clinical Isolate [Ye. G. Entina, S. B. Vakulenko; <i>ANTIBIOTIKI I KHIMioterapiya</i> , Vol 35 No 10, Oct 90]	82
Nucleotide Sequence of Gene aacC2 of E. coli Clinical Isolate [S. B. Vakulenko, Ye. G. Entina; <i>ANTIBIOTIKI I KHIMioterapiya</i> , Vol 35 No 10, Oct 90]	82

Hormonal Regulators of Calcium Metabolism Following Space Flights of Various Durations

917C0097A Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 24 No 4, Jul-Aug 90 (manuscript received 18 Jul 88)
pp 18-20

[Article by L. G. Pozharskaya and V. B. Noskov]

UDC 629.78:612.015.31:546.41/.06:612.441+612.447

[Abstract] The degree of parathormone, calcitonin, and gastrin system activity depending on the duration of weightlessness conditions was compared in 19 cosmonauts, 12 of which had seven-day flights, and 7 of which had flights lasting from 150 - 237 days. Blood samples were drawn 30 days before departure and 1, 7, and more days following arrival with the parathormone, calcitonin, and gastrin concentrations calculated using standard commercial test kits. Members of the short-term flight group exhibited a 45 percent average elevation in calcitonin, and a 44 percent gastrin content increase, while parathormone levels remained essentially unchanged. In members of the long-term flight group, parathormone levels were quite elevated and did not return to normal until 45 days after landing. Calcitonin levels were substantially depressed and in some subjects did not return to baseline levels by the end of the research period (45 days after landing). Gastrin levels were 3.3 times higher than pre-flight concentrations, and normalized within 45 days after returning to earth. The results demonstrated that parathormone and calcitonin help maintain calcium homeostasis by their opposite effects on calcium transport in the intestines and kidneys. The findings suggest that one of the reasons for hypergastrinemia following space flight may be the elevated parathormone level and abrupt decrease in calcitonin production. Furthermore, it is probable that the specific weight of the different components of the system maintaining calcium homeostasis varies depending on the duration of weightlessness and functional activity of the related regulatory systems. Tables 2; references 13: 8 Russian, 5 Western.

Computer Tomography Measurement of Vertebral Bones and Muscles After Extended Manned Space Flights

917C0097B Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 24 No 4, Jul-Aug 90 (manuscript received 14 Jun 89) pp 20-21

[Article by V. S. Oganov, K. Kann, A. S. Rakhmanov, and S. K. Ternovoy (USSR, USA)]

UDC 629.78:[612.75+612.74

[Abstract] Computer tomography was employed to measure the mineral density of lumbar vertebrae spongy tissue and lumbar muscle mineral volume and density in

four cosmonauts 1 - 3 months prior to and 20 - 27 days following extended space flights (5 and 7 months). The results demonstrated a 7.8 percent decrease in calcium density in the posterior vertebral bodies and a 4.4 percent decrease in spinal muscle volume. Studies on volunteers on earth demonstrated a decrease in mineral density in only 10 percent of the subjects. The lack of changes in some of the subjects in both groups was attributed to the effectiveness of preventive measures and defense mechanisms of the muscles and bones. The results demonstrated that the changes in bones and muscles were not dependent on the length of flight and that physical exercise did not completely prevent unfavorable changes. These data are of interest in assessing the risk of developing osteoporosis and the potential the skeleton has of losing its strength in conditions of weightlessness. Suggestions are also made for further studies on bone metabolism during space flights. Tables 1; references 11: 5 Russian, 6 Western.

Functional Activity of Hypophyseal-Thyroid System During 370-Day Antiorthostatic Hypokinesia

917C0097C Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 24 No 4, Jul-Aug 90 (manuscript received 19 Apr 89) pp 28-30

[Article by Ye. N. Kabitskiy]

UDC 612.432+612.441/.06:612.766.2

[Abstract] Biochemical investigations of the hypophyseal-thyroid system were conducted on 10 healthy male volunteers at -5° antiorthostatic hypokinesia. The principal means of preventing tissue degeneration was physical exercise while lying down. Group A began exercising on day 20 of the experiment, while group B began 100 days later. The 11 blood samples taken throughout the experiment were used to calculate the concentrations of thyrotropic hormone of the adenohipophysis, free thyroxin (FT₄) bound with thyroxin (T₄), and triiodothreonine (T₃). Radioimmunologic assay data detected no change in T₄ concentrations and only a partial decrease in thyrotropic hormone. The data on FT₄ suggest that inhibitory dissociation of the protein-hormone bond occurs during antiorthostatic hypokinesia. The results demonstrated that the decreased concentrations of T₃ observed during antiorthostatic hypokinesia may reflect a decrease in plastic metabolism. The data also indicate that depression of T₃ and FT₄ levels is due to enhanced rates of utilization of these hormones by tissues in connection with increased motor activity and anaerobic processes. These findings suggest that exercise in conjunction with antiorthostatic hypokinesia decreases the role of the humoral factor in activation of the thyroid by the adenohipophysis. This leads to a slight decrease in thyroid activity which is manifest as a decrease in FT₄ and T₃ concentrations in the blood. Furthermore, these

findings also demonstrated that exercise had no substantial effect on the functional activity of the hypophysis and thyroid. Figures 1; references 15: 7 Russian, 8 Western.

Changes in Rheologic Indices of Blood and Hemodynamics During 14-Day Antiorthostatic Hypokinesia

917C0097D Moscow KOSMICHESKAYA BIOLOGIYA I LAVIAKOSMICHESKAYA MEDITSINA in Russian Vol 24 No 4, Jul-Aug 90 (manuscript received 28 Sep 88) pp 30-32

[Article by A. P. Ivanov, I. B. Goncharov, and L. G. Repenkova]

UDC 612.117.2+612.13].06:612.766.2

[Abstract] Rheologic indices of the blood and hemodynamics were compared in nine essentially healthy men aged 25 - 42 years during various stages of 14-day antiorthostatic hypokinesia at -8° . Blood was drawn from the cubital vein on days 3, 7, and 14 of antiorthostatic hypokinesia and exhibited a 124.4 percent increase in Caisson blood viscosity, a 25.9 percent decrease in stroke volume, a 25.5 percent decrease in minute circulating volume, and a 23.6 percent increase in total peripheral resistance. These data suggest that there is a close relationship between central hemodynamic and rheologic parameter indices in antiorthostatic hypokinesia. The negative correlation relationship between total peripheral resistance and the dynamic viscosity of the blood is apparently associated with an increase in total peripheral resistance and blood viscosity as a result of slower circulation. Stases develop in the venous and capillary sections of the peripheral vascular system, and some of the formed elements of the blood are excluded from active circulation. All of these effects result in the additional opening of arteriovenous anastomoses in order to support adequate stroke and minute volumes. It is hoped that these studies will contribute to an understanding of how to control high blood viscosity, one of the risk factors of developing ischemic heart disease. Tables 2; references 19: 12 Russian, 7 Western.

Higher Plants as Part of Biological Human Life Support System

917C0097H Moscow KOSMICHESKAYA BIOLOGIYA I LAVIAKOSMICHESKAYA MEDITSINA in Russian Vol 24 No 4, Jul-Aug 90 (manuscript received 30 May 88) pp 40-43

[Article by I. Ye. Ivanova, T. A. Derendyayeva, T. P. Alekhina, and Yu. I. Shaydorov]

UDC 574.685:582.31

[Abstract] The functional characteristics of a man-plant-mineralization system were studied using higher

plants that perform a photoautotrophic role with *Chlorella* in a biological life support system. Wheat, peas, carrots, beets, cabbage, etc., were hydroponically cultivated in a winter garden and periodically given nutrients. The plants were cultivated for 6 months at 22 - 25°C, 55 - 70 percent relative humidity, with 24-hour per day lighting of 60 - 80 W/m² for the vegetables and 125 - 185 W/m² for the wheat. The plants demonstrated maximum productivity during days 70 - 100 of the experimental period, when mineralization products, drying of organic waste, and human and algal waste products all acted on the plants. The increase in the edible biomass of all the vegetables except the carrots was less than in the control group. Calculations of the vegetable contents of sugars, cellulose, ascorbic acid, and carotene (carrots only) demonstrated a 2.5-fold increase in vitamin C content in carrots, and a 2.2-fold increase in vitamin C and fructose in beets, with a 2-fold decrease in glucose and sucrose in the latter. The cellulose content of the peas also decreased by 13 percent. These results demonstrated that higher plants and *Chlorella* are compatible in a common atmosphere. It was also shown that the nutritive solutions given to the plants did not increase plant productivity. The reasons for the low productivity of the plants in a closed system remain inexplicable and thus require further study. Figures 1; tables 3; references 18: Russian.

Biochemical Aspects of Human Adaptation to Combined Effect of Antiorthostasis, Decreased Barometric Pressure, and Increased Oxygen Content

917C0097J Moscow KOSMICHESKAYA BIOLOGIYA I LAVIAKOSMICHESKAYA MEDITSINA in Russian Vol 24 No 4, Jul-Aug 90 (manuscript received 15 Apr 88) pp 56-57

[Article by T. N. Balandina, Ye. I. Nikitin, Ye. A. Kovalenko, and V. P. Savina]

UDC 612.273.1+612.76.014.477+612.275].014.49

[Abstract] The effects of relatively slight hyperoxia (pO₂ of 300 mm Hg) for 5 h and -8° antiorthostasis were assessed on seven men aged 25 - 35 years in an altitude chamber set at 7,100 m. The test subjects were also exposed to thermal (37°C) and physical stress (600 kg/m/min) for 5 min in the first, third, and fifth hours in the chamber and for 25 min also during the fifth hour. Venous blood was drawn before and after each trial for purposes of calculating malonic dialdehyde and self-induced lipid peroxidation levels. The results demonstrated that during the five-hour antiorthostatic period without exertion, erythrocytic catalase activity activated the protective antioxidant system, while the formation of self-induced lipid peroxidation products decreased. However, in five-hour antiorthostasis with exertion, the opposite was observed, i.e., normalization of metabolism. The results of the biochemical investigations as a whole suggest that in 5 h of antiorthostasis at -8° without exertion and with a pO₂ of 300 mm Hg there is an aspect

of stressing erythrocyte metabolism and compensating reactions. It was established that physical exercise in both regimens stabilizes the metabolic equilibrium that was disturbed in the cells, which is reflected in retention of the structural integrity of the erythrocyte membrane.

In addition, considering the degree of expression of the changes observed and signs of reparations of the erythrocyte membrane, these manifestations are judged to be functionally somewhat reversible, structural changes. Tables 2; references 5: 4 Russian, 1 Western.

Production of Verticillin Bioinsecticide

917C0028A Moscow ZASHCHITA RASTENIY
in Russian No 6, Jun 90 pp 20-21

[Article by Ye. F. Solovey, senior scientific associate, VNIIBMZR [All-Union Scientific Research Institute for Biological Methods in Plant Protection]]

UDC 632.937

[Text] Verticillin is a biopreparation based upon the spores from the *Verticillium* fungus. It is used against glasshouse whitefly *Trialeurodes vaporariorum* in hothouses. It is produced in biological laboratories by the surface cultivation of the fungus on barley or in a liquid medium in the form of a spore-micellar film. After washing the conidia from the surface of the nutrient substrate, one obtains a working suspension that is used to treat plants infested by whiteflies. This method for obtaining the preparation is simple and available. However, because of low productivity and the lack of biological laboratories and equipment, it is not possible to produce the preparation in the quantities needed for plant protection in the state and private sectors.

Our method for sub-surface cultivation can be carried out at microbiological factories and would make it possible to reliably control the quality of the preparation (something impossible at local biological laboratories). It would free sizable numbers of people engaged primarily in manual labor producing the preparation. Most importantly, it would meet agricultural demand for verticillin. This is especially important in view of the ecological situation in our country resulting from the intensive use of chemicals and of the need to convert to primarily biological methods of plant protection in covered areas.

Joint research with associates at the Berdsk chemical plant, begun in 1985, resulted in the development of a technology for verticillin production in this enterprise, using the sub-surface method for cultivating *Verticillium*. This research produced numerous samples of the preparation from various nutrient media using additives to prolong the life of the blastospores. Experimental batches of the preparation were obtained for testing in commercial hothouses: in 1986—170, in 1987—250, and in 1989—210 kilograms.

Verticillin is a cream-colored powder with a faint fungal smell. It is easily mixed with water and is not toxic to plants or warm-blooded animals.

Its main active component is blastospores. The preparation's quality depends upon their protection. It was discovered that under the most favorable storage conditions for the long term survival of blastospores (in closed polyethylene packages at temperatures of 4 - 6°C for 2.5 - 3 years), the spores do not lose their biological activity. At 24 - 26°C the number of living blastospores drops sharply even after 6 months storage.

In studying batches of the preparation using titrations of vital spores and different additives and nutrient media composition we noted considerable variation in their biological activity. Even at low temperatures some samples became inactive in less than 6 months. In verticillin produced in 1987 the number of living blastospores was at the previous level of magnitude even after 32 months. Samples produced in 1989 are still being studied.

The biological activity of the preparation was tested at experimental hothouses operated by VNIIBMZR and at commercial hothouses in Kislovodsk, Alma-Ata, Stavropol, Sochi, Krasnodar, Kiev, Kalinin, Nalchik, Voronezh, Cheboksar and Kishinev. (See the table).

Results of Testing Verticillin Against Glasshouse Whitefly on Cucumbers (application rate of 7 kg per 1,000 liters of water) in Commercial Hothouses

Test location	May 1986	September 1986	Percent of larvae killed	Humidity (percent)	Percent of larvae killed			Humidity (percent)
	Average	Per running meter	Maximum	c Average	Per running meter	Maximum		
Kislovodsk	55	0	100	74-82	—	—	—	—
Alma-Ata	90	57	100	74-94	71	62	89	80-86
Stavropol	52	25	90	75-82	24	6	40	62-82
Sochi	82	63	89	57-95	—	—	—	—
Krasnodar	78	74	82	73-87	—	—	—	—
Kiev	—	—	—	—	77	51	95	80-85
Kalinin	96	69	100	74-94	75	52	100	80-92
Nalchik	90	35	97	80-95	86	56	96	79-88
Voronezh	77	69	88	70-91	—	—	—	—
Cheboksary	65	11	100	78-88	—	—	—	—
Kishinev	74	54	91	78-89	—	—	—	—

The preparations were soaked in water for 24 hours to swell the spores. After this a suspension was prepared (2 kg of verticillin per 1,000 liters of water) and sprayed on cucumber plants infested by whitefly larvae. After treatment the soil and walkways were thoroughly watered and it was attempted to maintain relative humidity above 85 percent. However, it was not possible to maintain such high levels at all hothouses. This had an effect upon preparation effectiveness. As is known, when a hothouse is heated the moisture in the air is very unevenly distributed throughout the space. It is particularly dry along the perimeter near the heating system, where the first pests often appear. It should also be noted that preparation effectiveness varies from 0 - 100 percent depending upon the distance between the leaves and the moisture source. Plant treatment in the spring and the fall showed that if the optimal humidity is maintained

this biological agent can be successfully used on any crop rotation.

A batch of verticillin obtained in 1987 was tested in commercial hothouses in Nalchik, Alma-Ata, Kalinin, Cheboksar, Stavropol and Kishinev, where it was used on cucumbers throughout the entire vegetative growth period. It made possible reductions in, or the complete elimination of, chemical applications.

Thus, this research shows that verticillin can be produced not only in biological laboratories, but also in factories of the microbiological industry. The equipment for this is available. So far, however, neither the agroprom nor the microbiological industry has shown any genuine interest in producing this biological preparation.

Structure of recA Gene of *Pseudomonas aeruginosa*

917C01191 Moscow BIOORGANICHESKAYA KIMIYA in Russian Vol 16 No 9, Sep 90 (manuscript received 09 Feb 88; in final form 20 May 90) pp 1177-1182

[Article by V. M. Kryukov, Ye. N. Zaytsev*, N. N. Kuzmin and A. A. Bayev, Institute of Biochemistry and Physiology of Microorganisms, Pushchino, Moscow Oblast, and *Leningrad Institute of Nuclear Physics (now B. P. Konstantinov, Gatchina, USSR Academy of Sciences)]

UDC 579.84.11.579.25.113.57.113.5

[Abstract] As part of a program toward a better understanding of the evolution of the recA gene, sequencing was performed on the recA gene of *Pseudomonas aeruginosa*. Analysis of a previously cloned 1206 bp fragment bearing the recA gene showed a consensus AGGA sequence at a distance of 5 nucleotides from the initiation codon ATG, complementary to the 3'-ends of 16S RNA of both *Ps. aeruginosa* and *E. coli*. An open reading frame was identified that corresponded to a 36808 D protein that displayed high homology (70 percent) with the corresponding *E. coli* protein. However, DNA homology between *E. coli* and *Ps. aeruginosa* was only on the order of 67.2 percent because of the high G+C ratio in the latter. Studies with nuclease S1 and reverse transcriptase showed that, in both genera, transcription is initiated from nucleotides T89 and A90, with the initiation site preceded by AATAATA in *Ps. aeruginosa* versus TATAATA in the -10 promoter region of *E. coli*. Region -35, however, failed to show a similar degree of analogy. The *Ps. aeruginosa* protein encoded by recA gene is shorter by 7 amino acids than the *E. coli* protein and differs from the latter at 108 positions, mostly in the C-terminal portion of the molecule. Consequently, the C-terminal region can be assumed to be of secondary importance in the function of the recA protein. Figures 3; tables 1; references 21; 1 Russian, 20 Western

Chemical Reactions in Double-Stranded Nucleic Acids. Part 10. Kinetics of Oligomer Ligation by Water-Soluble Carbodiimides

917C0119B Moscow BIOORGANICHESKAYA KIMIYA in Russian Vol 16 No 9, Sep 90 (manuscript received 30 Oct 89) pp 1183-1194

[Article by N. G. Dolinnaya, A. V. Tsytovich, V. N. Sergeyev, M. N. Gertsyuk* and Z. A. Shabarova, Chemical Faculty, Moscow State University; *Institute of Bioorganic Chemistry, Ukrainian SSR Academy of Sciences, Kiev]

UDC 577.113.4.541.124

[Abstract] An analysis was conducted on the structural-kinetic relationships in ligation of one strand of an

oligonucleotide duplex by 11 water-soluble carbodiimides. Reactivity parameter showed the importance of substituents on atoms N1 and N3 of the carbodiimide, and of the number of methylene bridges on the rate of single-strand ligation. Highly efficient carbodiimides did not undergo cyclization or incorporate a phenyl radical. A kinetic parameter based on the ratio of reaction rates was derived which was independent of the nature of the carbodiimide but sensitive to oligonucleotide structure in measuring the rate of activation of phosphate groups. Figures 6; tables 1; references 12; 8 Russian, 4 Western

Chemical Reactions in Double-Stranded Nucleic Acids. Part 11. Correlation Between Kinetics of Chemical Ligation of DNA Duplexes and DNA Modification at Reaction Site

917C0119C Moscow BIOORGANICHESKAYA KIMIYA in Russian Vol 16 No 9, Sep 90 (manuscript received 30 Oct 89) pp 1195-1202

[Article by N. G. Dolinnaya, A. V. Tsytovich, S. G. Levosyan, V. N. Sergeyev and Z. A. Shabarova, Chemical Faculty, Moscow State University]

UDC 577.113.4

[Abstract] An assessment was conducted on the rate of chemical ligation of single oligonucleotide strands in a DNA duplex by 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide in the face of various chemical modifications of the DNA target. Modifications at the site of the single-strand breaks consisted of alterations in the position of the phosphate group (5' or 3'), replacement of 3'-thymidine by ribouridine or a nucleoside with reversed configuration at C2'- or C3'-furanose, introduction of extraneous purine or pyrimidine monomers on the donor or acceptor ends, and replacement of G:C pairs by a noncomplementary G:G pair one base away from the break. The results of ligation kinetics and the melting curves of the products showed that such changes had variable effects. Distortions induced by G:G pairs do not affect orientation of adjacent structural features and had no effect on the rate of ligation, while extraneous base pairs reduced the yield and rate of reaction about 2-fold. Efficiency was also shown to be reduced in duplexes bearing a ribouridine substituent, presumably due to profound configurational distortions in the 3'-terminus. Ligation was almost completely precluded by C2'- and C3'-furanose inversions. These observations delineated some of the structural parameters important in chemical ligation, many of which have been shown to hold true for enzymatic ligation. Figures 9; tables 3; references 20; 11 Russian, 9 Western

Structure of Photosynthetic Reaction Center of Green Thermophilic Bacterium *Chloroflexus aurantiacus*

917C0119D Moscow BIOORGANICHESKAYA KIMIYA in Russian Vol 16 No 9, Sep 90 (manuscript received 04 Nov 89) pp 1218-1235

[Article by M. A. Kutuzov, B. Ye. Shmukler, A. A. Zargarov, N. N. Telezhinskaya, N. B. Levina, A. S.

Zolotarev and N. G. Abdulayev, Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow]

UDC 577.113.8

[Abstract] A detailed analysis was conducted on the polypeptide components of photosynthetic reaction center (RC) of *Chloroflexus aurantiacus*, employing conventional protein chemistry as well as genetic engineering. SDS electrophoresis led to the identification of a 47kD dimer, although calculations based on amino acid composition yielded a MW of approximately 60 kD. Serine was identified as the sole N-terminal amino acid, while valine and proline were determined to be the C-terminal acids. In analogy to the RCs of purple bacteria the subunits were designated as L (35014 D) and M (34982 D) subunits. On the basis of hydrophobicity, absorption spectra, amino acid composition and information on tertiary structure, a putative disposition of the polypeptides in the photosynthetic membranes of *C. aurantiacus* is proposed. In addition, a tentative conclusion has been reached that differences in the N-terminal end of the peptides account for greater thermal stability of *C. aurantiacus* RC in comparison with purple bacteria. In *C. aurantiacus* the N-terminal end of the L subunit are 30 amino acids longer and consist of 2-3 times as many charged amino acids. Studies with *C. aurantiacus* genome bank showed that genes encoding the L and M subunits represent independent operons, again differing from the situation in the purple bacteria. Figures 6; references 46: 6 Russian, 40 Western.

Synthesis and Reactivity of Novel Water-Soluble Carbodiimides

917C0119E Moscow BIOORGANICHESKAYA KIMIYA in Russian Vol 16 No 9, Sep 90 (manuscript received 14 Mar 89; in final form 18 Jan 90) pp 1268-1276

[Article by M. N. Gertsyuk, V. N. Sergeyev*, A. V. Tsytoich*, N. G. Dolinnaya* and V. P. Kukhar, Institute of Bioorganic Chemistry, Ukrainian SSR Academy of Sciences, Kiev; *Chemical Faculty, Moscow State University]

UDC 547.491.6.05

[Abstract] Eleven analogs of 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide (I) were synthesized for IR spectrometric studies on their ring-chain tautomerization. The congeners of I differed in substituents on the N1 atom (methyl, ethyl or phenyl group), the number of methylene bridges at N3 (2 or 3), and the nature of the amino group (tertiary or quaternary). In general the resultant data showed that congeners with 2 methylene bridges tend to form 5-membered rings and lead to loss of reactivity with nucleophilic reagents. Figures 5; tables 4; references 7: 2 Russian, 5 Western.

Peptide With Universal Tryptophanyl-tRNA Synthase Epitope

917C0119I Moscow BIOORGANICHESKAYA KIMIYA in Russian Vol 16 No 9, Sep 90 (manuscript received 14 Mar 89; in final form 06 Dec 89) pp 1289-1296

[Article by I. A. Zargarova, A. A. Zargarov*, I. A. Bolotina (dec), S. I. Beresien and O. O. Favorov, Institutes of Molecular Biology imeni V. A. Engelgardt and of Bioorganic Chemistry imeni I. M. Shemyakin USSR Academy of Sciences, Moscow]

UDC 577.152.611.4.083.3

[Abstract] An 18 amino acid peptide, designated TSC-O-22, was isolated from bovine pancreatic hydrolysate and was shown to contain the universal tryptophanyl-tRNA synthase epitope characteristic of prokaryotes, eukaryotes and archaebacteria in studies with specific monoclonal antibodies (MA). The peptide (His-Ser-Phe-Pro-Ala-Ile-Asn-Gln-Phe-Ala-Ala-Pro-Ser-Gln-Ile-Arg), as well as its congener with an additional Arg moiety at its N-terminus, reacted equally well with the same MA in immunoassays when immobilized on planchettes. In addition, affinity constants obtained with the native enzyme antigen ($1.4 \times 10^9 \text{ M}^{-1}$) and the peptide ($3.0 \times 10^9 \text{ M}^{-1}$) in noncompetitive immunoassays were quite close. The latter finding indicates that TSC-O-22 represents the major antigenic configuration of the enzyme. The amino acid sequence of TSC-O-22 suggests the presence of beta-turn(s) and a beta-sheet configuration. However, CD spectra in the far UV band of the peptide dissolved in water yielded information indicating that 16 percent (3) of the amino acids are involved in the beta-turn(s) and only 8 percent (2) in the beta-sheet, while the rest of the molecule is unstructured. Figures 6; tables 1; references 30: 4 Russian, 26 Western.

Replicative Complex of Tick-Borne Encephalitis Virus (TBEV). Part 2. Effects of Envelope Protein E (EPE) and Anti-EPE Antibody on In Vitro RNA Synthesis

917C0119G Moscow BIOORGANICHESKAYA KIMIYA in Russian Vol 16 No 9, Sep 90 (manuscript received 04 Dec 89) pp 1297-1309

[Article by O. V. Morozova, N. A. Belvayskaya*, L. E. Matveyev, E. A. Kvetkova* and A. G. Pletnev, Novosibirsk Institute of Bioorganic Chemistry, Siberian Department, USSR Academy of Sciences, *Omsk Institute of Regional Infections, RSFSR Ministry of Health]

UDC 577.152.277:577.112.4

[Abstract] In vitro studies employing SPEV tissue culture were performed on the involvement of EPE in TBEV replication. The experimental technique involved

addition of FPI and anti-FPI monoclonal and polyclonal antibodies and assessment of RNA synthesis. Addition of FPI led to a marked inhibition of RNA synthesis, whereas addition of the antibody enhanced RNA synthesis. Analysis of temporal parameters suggested that the inhibitory mechanism of action of FPI involved initiation of RNA synthesis, presumably due to binding of FPI to the template or the replicative complex. Figures 2; references 3. 2 Russian, 1 Western.

Synthesis of Histidine and Carnosine Phosphoanalogs

917C0119H Moscow BIOORGANICHI SKIY I KHIMIY I in Russian Vol 16 No 9, Sep 90 (manuscript received 19 Dec 89, in final form 09 Apr 90) pp 1290-1293

[Article by A. R. Khomudov, Institute of Biochemistry imeni A. N. Bakh, USSR Academy of Sciences, Moscow]

UDC 547.466:547.24

[Abstract] Synthesis of phosphoanalogs of histidine and the dipeptide carnosine (Ala-His) was commenced by transformation of histidine into an oxime of imidazole-acetaldehyde (I) by treatment with hydrogen peroxide in the presence of Na₂. Subsequently, I was treated with hypophosphorous acid to give β -imidazolyl- α -aminoethylphosphonous acid (II), followed by conversion of II to β -Ala-II by reaction of N-Z- β -Ala with II and elimination of the Z group by HBr. The corresponding phosphonic acids were prepared by oxidation with SO₂Cl₂ in glacial acetic acid. Tables 1; references 14. 3 Russian, 11 Western.

Exposure of HIV-1 gp41 Transmembrane Protein Epitopes on Surface of Hepatitis B Core Antigen Capsids

917C0120 Moscow BIOORGANICHI SKIY I KHIMIY I in Russian Vol 16 No 9, Sep 90 (Signed to press 01 Feb 90) pp 1283-1286

[Article by R. Ulrikh, G. P. Borisova, R. Mering et al. Institute of Medical Virology, Department of Medicine, University imeni Humboldt (Sharite), Berlin, GDR; Department of Molecular Biology, Institute of Organic Synthesis, Latvian Academy of Sciences, Riga; Institute of Microbiology imeni A. Kirshenshteyn, Latvian

Academy of Sciences, Riga; Experimental Plant of the Institute of Organic Synthesis, Riga]

UDC 578.112.083.3.578.2.24.21

[Abstract] The transmembrane protein gp41 of HIV-1 served as the source of epitopes for exposure. Plasmid pHbc1315, carrying the core-antigen gene with poly-linker segment EcoRV-ClaI-PvuI, introduced into site MspI, which overlaps Pro¹⁴⁴, served as the "exposure vector". Insertion of 52 amino acid sequences of transmembrane protein gp41 of HIV-1, containing amino acid residues 78-129 of gp41 or 596-647 of Env in the Pro¹⁴⁴ position of the hepatitis B core antigen (HBcAg) caused formation of chimeric capsids. The capsids retained the morphology of intact HBcAg but exposed major HIV-1 epitopes on their outer surface, localized in the inserted gp41 fragment. The chimeric capsids possessed not only antigenic properties of gp41 but also the immunogenicity typical of it. The localization of gp41 epitopes on the capsids did not depend on the presence or absence of the arginine-rich 39 amino acid C-terminus of HBcAg. Chimeric capsids based on HBcAg may be used as components of diagnostics and vaccines. Figures 2; references 15. 3 Russian, 12 Western.

Chemical Reactions in Duplex DNA. Part 12. Novel Gene Assembly Strategy

917C0121 Moscow BIOORGANICHI SKIY I KHIMIY I in Russian Vol 16 No 9, Sep 90 (manuscript received 26 Feb 90) pp 1287-1289

[Article by Z. A. Shabarova, I. N. Merenkova, T. S. Oretskaya and N. I. Sokolova, Chemical Faculty and Interfaculty Special problems Scientific Research Laboratory of Molecular Biology and Bioorganic Chemistry imeni A. N. Belozerskiy, Moscow State university]

UDC 577.113.4

[Abstract] A 183 bp synthetic gene was assembled, using BrCN to link four 35-53-bp oligodeoxynucleotide fragments on a complementary strand. The resultant duplex DNA incorporated a strong promoter (analog of λ P_R, regions OR1 and OR2), initiator (SD+ initiation codon ATG), and transcription terminator (T_{td}). Expression of this gene is anticipated to yield a 130-mer mRNA and a 16 amino acid peptide. Figures 2; references 10. 2 Russian, 8 Western.

Effects of Ultraviolet Light on Bacteriorhodopsin

917C0100C Moscow *RADIOBIOLOGIYA in Russian*
Vol 30 No 4, Jul-Aug 90 pp 506-511

[Article by L. S. Broun, A. A. Kononenko, T. B. Prptaspa, I. B. Fedorovich and S. K. Chamorovskiy, Biological Faculty, Moscow State University; Institute of Chemical Physics, USSR Academy of Sciences, Moscow]

UDC 577.391.612.014.44

[Abstract] An analysis was conducted on the effects of UV-B light (280 - 320 nm) on bacteriorhodopsin (BR)

isolated as purple membrane suspension from *H. halobium* 353-P, in view of the potential applications of BR in biotechnology. Analysis of the spectral changes showed that at UV-B doses = / < 15 kJ/m² induced a bathochromic shift in the major absorption band, while at > 15 kJ/m² destruction of the chromophoric groups led to bleaching of the α (major) and γ (UV) bands resulting in the appearance of a new absorption band at 340 - 380 nm. Subsequently, the latter band also disappeared. Dehydration was shown to decelerate the process of UV-B mediated destruction of BR. Since BR fluorescence is primarily due to tryptophanyl residues, the bathochromic shift was attributed to ionization of two of these moieties. Figures 4; references 25; 2 Russian, 23 Western.

Preclinical Trials With Soviet Recombinant Human Interferon-A2 (Reaferon)

917C0035G Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOLOGII* in Russian No 6, Jun 90 (manuscript received 12 Jun 89) pp 93-97

[Article by Yu. T. Kalinin, A. A. Vorobyev, V. A. Bumyalis, L. A. Denisov, V. V. Partenov, A. V. Klenova, A. A. Yanylaytis, F. I. Yershov, V. I. Marchenko and V. V. Malinovskaya, 'Biopreparat' Main Administration (Moscow) and Institute of Immunology (Moscow Oblast) USSR Ministry of Medical and Microbiological Industry; 1st Moscow Medical Institute (mem) I. M. Sechenov, USSR Ministry of Health, Scientific Research Institute of Epidemiology and Microbiology (mem) N. I. Gamaleya, USSR Academy of Medical Sciences]

UDC 615.339.578.245].038

[Abstract] A brief comparison is presented on reaferon and two American recombinant interferons (Intron A and Roferon), which demonstrates that the Soviet drug is on par with the Western drugs in terms of safety, purity, and activity. Reaferon is produced by genetically engineered *Pseudomonas putida* VGi-84 bearing the recombinant plasmid pVGi-3, in which the human gene is under the control of gene D of bacteriophage π X-174. The production is 10^9 IU/ml of bacterial suspension. Reaferon has a MW of 18 kD and is available in 99 percent purity. Tables 1, references 6: 3 Russian, 3 Western.

Increased Cholera Incidence Due to Contaminated Water

917C00091 Moscow IZVESTIYA in Russian 23 Aug 90
Morning Edition p 6

[Article by I. Dmitriyeva: "The Quiet Don Threatens Cholera"]

[Text] Worry over the cholera outbreak in Stavropol barely subsided before another piece of news dumbfounded the country: Cholera in Rostov! Could it really be that it is once again spreading despite all of the measures, all of the efforts to retrace the steps of hundreds of people who had come in contact with the infection, and to block its spread?

"No, this case is not associated with Stavropol's," said RSFSR Deputy Minister of Public Health Ye. Belyayev, chief state public health physician. "The Stavropol cholera focus was eliminated. We were able to find and examine not only registered guests at Rodnik Campground but also guests who had not registered with any organized groups."

"How was that possible?"

"Because of the mass media. People found out about the threat of the epidemic from the newspapers and television, they allowed themselves to be tested, and they helped to find others. For example several campers from Krasnodar staying at the Rodnik Campground—then stay had not been noticed by anyone—themselves went to their doctors, thus preventing spread of infection. Unfortunately, they were not spared of cholera infection. Consequently we doctors are very grateful to journalists for their help, and for the objective and efficiently communicated information."

It's a rare thing for someone to praise journalists. But let's return to the Rostov story. A certain inhabitant of the city of Kamensk, Rostov Oblast, came to Koluzavevo Homestead for the funeral of her tragically departed husband. Soon after the memorial service she felt poorly, but she did not seek medical care. A few days later she had to be taken by ambulance to the hospital in Rostov in extremely serious condition. The doctors (alerted by the situation in Stavropol) suspected cholera. And that is what they soon confirmed.

Inhabitants of the homestead—around 400 persons—were examined. Four were found to be ill, and five were discovered to be carriers of the infection; moreover eight of these nine persons were members of the same family. One other patient had not been in contact with this family, but like her neighbors, she used water from the Don without boiling it first. Moreover, water from the river was stored in containers in the heat of the blazing sun, where the vibrio enjoyed ideal conditions for swift duplication. All of this has been confirmed: The people were infected by water from the Don, although subsequent regular laboratory tests did not reveal the cholera vibrio in it.

Once in a while, serious infection does make itself known in Rostov. There's nothing surprising in that—over 80,000 cubic meters of sewage are dumped daily by the city into the river practically untreated. The treatment plants are overloaded, while construction of new ones is off schedule. This is why favorable conditions for development of all kinds of infections are being created within the city limits below the city's sewage discharge. The matter of building treatment plants has not been resolved for many years now—back since the times of the previous outbreaks of the 1970s. Doctors go about extinguishing the outbreaks of "fire," but the embers of the chronic focus glow continually.

"Does this mean, then, that unrevealed vibrio carriers are living somewhere in Rostov itself?"

"Man cannot be the bearer of a vibrio for long," continued Ye. Belyayev. "The vibrio quickly perishes, and the body in a sense undergoes self-purification. But the source of infection may appear at any moment. Rostov is a large city, in which there are many foreign students, including those from regions where cholera outbreaks are perpetually recorded. The danger of its 'export' exists all the time, all the more so because the seventh pandemic of cholera, which began in the world in 1961, has not yet come to an end. Its echoes are still being heard in our country as well. Since then much of the people of our country have suffered this disease. Two years ago four athletes brought Ogawa-type El Tor vibrio, the most aggressive and viable, from Cairo. Much effort had to be taken at that time to keep the infection from spreading through Moscow, the Moscow suburbs and Leningrad. By the way, quite recently we once again 'trapped' cholera vibrio in the Moskva River. Last year we isolated it 13 times in six regions of the republic, while this year we have already isolated it 12 times in five areas. The year has not even ended, after all, and one of the most unfavorable months—September—is still to come."

"And what do you do in such cases to keep an epidemic from happening?"

"We have developed special tactics, and our epidemic control measures include constantly monitoring the environment and water basins, examining the population in risk zones, finding persons who had come in contact with infection, conducting backyard inspections, disseminating information, posting warning signs and reminders, and so on. But none of our health education work can give a 100 percent guarantee against disease if no concern is given to the cleanliness of water basins. They are so contaminated that they have turned into incubators of all kinds of infections. Over 100 cases of paratyphus were registered in Tuva, there was an outbreak of dysentery in Barnaul, and many other examples can be cited. Intensive contamination of water basins results in contamination of tap water as well. Around 10 percent of it is contaminated in the water systems due to problems within them that cause sewage to be siphoned into water mains. The operating, sanitary and technical condition of water main and sewage facilities is a big

problem in our republic. Therefore although fear of serious infections can be contained quickly, we cannot say that the epidemiological situation is favorable."

"I remember the cholera outbreak of the 1970s—the losses were so staggering then! Watermelons and even roe had to be destroyed, and entire cities were quarantined."

"Today the losses are minimal. So they closed Rodnik Campground for a while (it had to be shut down anyway in order to repair the water system). So they obliterated the spring itself there, so that the uninformed wouldn't take water from it. There are some expenses associated with 'backtracking' and treatment, and that's all. Owing to their experience, professionalism and good, competent work, medical personnel are able to intercept cholera at its inception. And there have been no deaths from it, thank God. But how long will we have to continue playing the firemen?"

And so, although everything turned out all right in Rostov, there is no guarantee that such a situation will not arise in another place. Who's next?

Catastrophic Hepatitis Situation

917C0010A Moscow IZVESTIYA in Russian 16 Aug 90
Morning Edition p 3

[Article by S. Tutorskaya: "How to Deal With Hepatitis"]

[Text] In recent years the summer reports of epidemiologists more and more frequently recalled dispatches on lengthy battles dragging on with minor successes and growing losses. Doctors are now anxiously awaiting September—the time of peak incidence of viral hepatitis. Nor is the picture observed in August very pleasant.

In our country, says USSR Ministry of Health specialist G. Onishchenko, there are not less than five varieties of viral hepatitis. As we know, hepatitis B is the worst. It often has a lethal outcome. Survivors may become carriers of the virus (the infection transmission pathways are the same as for AIDS virus). One person in the world dies from hepatitis B every 15 seconds. Today this is the most dangerous viral disease, leaving even AIDS behind.

In our country the incidence of this severe form of hepatitis doubled in the last 10 years. Moreover, according to specialists, over two-thirds of all infections were the result of therapeutic and diagnostic procedures. In particular, up to 15 percent of the infected persons contracted the disease after transfusions of blood and its components.

This was only to be expected, since even in Moscow only 59 percent of the hospitals have centralized sterilization departments that can ensure dependable sterilization. The famous Hospital imeni Botkin, for example, does not have such a department.

Medical personnel themselves have begun speaking out evermore loudly about the catastrophic situation in hospitals in regard to all instruments, including ordinary syringes, and disinfecting and washing agents. It is impossible to ensure sterility in such conditions, they emphasize. And medical personnel can't solve the problem alone.

According to information of the USSR Ministry of Health, the testing of the blood of donors for hepatitis B is poorly organized. Old, insufficiently sensitive methods are being employed. Highly sensitive diagnosticums are being produced in glaringly small quantities. Our country does have reliable diagnosticums, but the USSR Ministry of Medical Industry produces them in insufficient quantities, and instead supplies obsolete ones. And if this is so, then where is the total guarantee of the purity of donated blood?

Creating new conditions in our therapeutic institutions, ones corresponding to the requirements of the day and the century, is a matter of the utmost urgency, literally a matter of life and death. And this is, of course, something our new soviets need to concern themselves with.

As they say, misfortune begets misfortune. In the last few years, the quality of drinking water in the country's major cities deteriorated in relation to bacteriological indicators by a factor of 2 - 5. And the sanitation service can no longer guarantee that a glass of tap water will not be harmful. (For comparison, water in developed European countries is also often unsafe. It is boiled, or water of guaranteed purity is purchased in stores). Our unboiled water and, unfortunately, the products of our dairies often bring us yet another form of hepatitis— hepatitis A. It is also transmitted by unwashed hands.

The higher the sanitary and cultural level of a household and the cleaner food and water are, the lower is the danger of hepatitis A. Here is what that same G. Onishchenko said about this: Were there suddenly no physicians in Scandinavian countries, sharp growth of hepatitis, especially hepatitis A, would not occur. Hepatitis A strikes children predominantly. It does not kill, but it produces serious complications. Other hepatitis viruses of the same type, with the same transmission pathway and the same "juvenile" spectrum of action have been revealed.

Vaccines against hepatitis A and B are already available abroad. In order that they could successfully produce them here, enterprises of the Ministry of Medical Industry in Leningrad need imported equipment worth around 6 million in hard currency. However, when the discussion turned to its purchase, the industrialists were denied the money. And in the meantime the patients are waiting.

When will the morbidity curve stop climbing?

One million doses of hepatitis B vaccine purchased from a Belgian company will be used up quickly; newborn infants and medical personnel working in the "risk

zone" will receive immunizations. There can be no hope for the end of more and more new outbreaks of hepatitis until we first implement some social measures. For instance, rebuilding the water mains, subjecting population centers to sanitary cleansing, and monitoring food quality (in food companies of the West, around 40 percent of the personnel conduct such monitoring). Of course, the therapeutic institutions also need to be completely re-equipped, and sterile conditions must be observed religiously. All of this of course costs a great deal of money. But isn't there a price to pay for high incidence of hepatitis, after all? Without even discussing the moral loss, the economic loss for just 1 year is 628.8 million rubles. But the real losses are obviously even larger: Some oblasts and republics understate and conceal their morbidity statistics.

It is evident from one quick look at the measures that many departments and institutions, primarily of the Ministry of Food Industry and the Ministry of Medical Industry, the public health service, the soviets and the public must take notice of the cleanliness problem. Given the low level of hygiene prevailing today, any one of us might contract a serious ailment. Either we all save ourselves, or none of us will be saved.

Hepatitis in Uzbekistan

917C00134 Tashkent PRAIDA VOSTOK in Russian
28 Jul 90 p. 3

[Article by Murad Mukhammad-Dost: "Saffron Syndrome"]

[Text] It was called saffron disease in the East since ancient times. The beauty which we now attribute to the word was nonexistent then. It referred only to an external sign of an ailment: the saffron, or yellow, color of the patient's face. The present name of the disease—*sarik* [transliteration], which corresponds in all hues to the Russian *zheltukha* [jaundice]—established itself later on.

Disappointingly, for dozens of years, Uzbekistan has held first place for the number of cases of viral hepatitis. While the republic's inhabitants make up only 7 percent of the country's population, they contribute almost half of the union's statistics. There is practically not a single family here that has been spared of saffron disease.

Let me begin with examples close to me. One of the brothers in the family of my relatives suffered twice: He caught jaundice while harvesting cotton, and he was infected with serum hepatitis in the hospital while receiving injections. To this day he complains of liver pains, cursing medicine with a single word—"unwashed." His nephews and sister-in-law—the wife of his younger brother—had the disease as well.

I must admit that there was a time when I explained the woes of my relatives by the fact that they live in a distant kishlak. But an acquaintance of mine, S. Yakubov, the chief physician of Tashkent's tuberculosis dispensary,

found my conclusion disconcerting. "No, you're mistaken. Tashkent is not at all 'behind' the kishlaks. Seven of my grandsons have suffered hepatitis." And then he recalled the family of an associate, Professor S. Mukhamedov, who also had seven grandsons who were infected with jaundice. I decided not to interview the professor on learning that one of his grandsons could not be saved. This is despite the fact that Yakubov is an excellent phthisiologist and Professor Mukhamedov is one of the republic's best epidemiologists, and if they, these loving grandfathers, were unable to save their own youngsters, then.... my deep apologies to them for unwittingly opening up old wounds in making their names public for the sake of credibility.

People are gradually becoming accustomed to thinking of jaundice as an inescapable evil. Sort of like the situation in that fairy-tale city from which a cruel dragon carried away the inhabitants one at a time, while the rest obediently awaited their fate. Of course, in the tradition of this genre the tale has a happy ending—an enchanted knight appears, and rids the city of the dragon.

But in the case of jaundice, is there any hope for knights coming to the rescue? The medical assault forces that are regularly sent from the center to the biggest problem areas in the republic play this role in the opinion of some. This, of course, is an act of mercy of no small importance, but you must agree that it is a forced one, and frankly speaking, it is not at all the best reflection upon our public health system. In any case the geography of the disease is such that no assault forces of any kind will encompass it entirely.

I can hear the reproachful exclamations now. "You're creating panic. You're generalizing. How can you possibly arrive at such far-reaching conclusions from just a few personal and family examples?"

All right, let's set emotions aside. Let's consider the dry figures in a letter from Uzbek SSR Minister of Health S. M. Bakhramov, who graciously responded to my request for an update on things as they are. Here, then, are the statistics: The absolute number of cases of illness in the last 11 years—from 1979 to 1989—was 1,933,000. Of these, 1,663,002 cases were viral hepatitis A, and 269,998 cases were viral hepatitis B, referred to colloquially as serum hepatitis, that is, having its origin associated with dirty syringes.

Is glasnost alive and well? Let's not be too hasty. The data I have, which cover 15 years, indicate that 2,522,453 persons suffered viral hepatitis, including 305,443 persons with serum hepatitis. But neither our statistics nor those of the ministry can be said to be exhaustive. We are all aware that patient records have been manipulated for many long years in order to "improve upon the picture." Moreover the practice of anonymous treatment, which was to the liking of patients (a couple of rubles for a shot at home, and no red tape, nor, by the way, any guarantees against infection),

existed then, as it does now. Which is why some specialists offer a larger figure—up to 4 million jaundice patients in the last 15 years.

But lest we be accused of slander, we will work with official statistics only. According to data of the Uzbek SSR Ministry of Health, 10 percent of the republic's population has suffered the disease. That means that 1 out of every 10 persons is personally familiar with the accursed syndrome. The consequences of the disease include an unhealthy color of the face, agonizing pains in the liver, the need for sticking to a strict diet (which is burdensome when there is no choice of foods) and constant fear for one's children, including future ones.

Dare I think that the numerous decrees of the Ministry of Health and decisions of epidemiological councils regarding the fight against viral hepatitis were only peace offerings of just another crash campaign? Ministers, who came and went almost annually, and their deputies as well, have sincerely wished to put an end to jaundice (the sunsets of ministry careers have almost always coincided with peaks of this disease, by the way), and they had faith in the effectiveness of their resolutions and of their various memos—"intensify", "improve", "reach more people" and so on. But in the meantime, in the inner sanctums of agroindustrial concerns, or more precisely, in the most unreachable (in terms of glasnost) offices of Selkhozkhimiya, other resolutions were being written, pursuing entirely different goals, judging from the results. These were staggering results in more ways than one. The vigorous efforts of the chemists led to a situation where every hectare of celebrated Uzbek land now contains dozens of kilograms of toxic chemicals. And the poisoning is continuing in a geometric progression. One hundred thousand tons of pesticides and herbicides were used in 1988, while as many as 110,000 tons were used in 1989. Moreover these toxic chemicals were applied to all of 80 percent of worked land, and not just the fields on which cotton and other industrial crops are grown. What are we putting into our mouths?

Once I asked specialists at Selkhozkhimiya about the origin of the nitrates of which both young and old speak fearfully today. They explained to me condescendingly that Selkhozkhimiya had nothing to do with that—nitrogen, phosphorus and potassium, which are intended to stimulate plant development, you see, form completely harmless organic compounds. "Does this mean that we don't necessarily have to stick to any particular dose rate?" I asked timidly. The scientists reluctantly admitted: "Yes, it's better to apply nitrogen, phosphorus and potassium doses at a ratio of 2:1:0.8, since otherwise undesirable byproducts, like nitrates, might form." But then my question as to whether they had ever come across a single machine operator in real life who strictly metered out the mineral fertilizers he was applying remained unanswered. Apparently such an ideal machine operator does not exist in nature.

Anyway, it is generally impossible to have a discussion among equals with representatives of this self-assured

department. The moment you begin questioning the right of Selkhozkhimiya to interfere unpardonably in the biosphere, you are accused of being a retrograde, and then frightened to boot with the prospect of universal starvation, given the growing appetite of the people. Of course, I personally see no difference between dying from lack of food and dying from poisons slipping unobserved into the fruits and vegetables I buy every day. Consider how far things have gone: Toxic impurities are being detected in ever-growing quantities in mother's milk!

Consumption of mineral fertilizers in the country increased by a factor of 15 in the last quarter century. The amount by which the yields of agricultural crops have risen in response is a great secret, which each of us tries to fathom at our own dining tables. In the meantime the dubious "successes" of the chemists are making themselves known by way of the indicators of the struggle against viral hepatitis currently being initiated. The dynamics here are as follows: In 11 years the number of persons afflicted with the saffron ailment nearly tripled. What does this suggest? Are doctors putting up a weak fight, or have they laid down their arms altogether? No, they are honorably continuing about their business—they are treating the disease, but this is turning out to not be enough. When all effort is committed against the disease itself—that is, the consequence, and its causes are blind-sided, we can't expect anything else.

As we know, many of us have our own particular "threads" which, if followed, easily lead to the key to an understanding of particular actions. But does an entire ministry or department have such "threads"? Certainly! In the case of the chemists, they are the peasant farmer who is unable to follow their simple instructions when applying fertilizers to the fields. Or the threat of starvation in the event of abandonment of nitrogen-phosphorus-potassium top-dressings. As far as the Ministry of Health is concerned, it has its own particular "thread"—universal installation of water supplies and sewage systems, which is something the Ministry of Housing and Municipal Services is supposed to achieve but can't. But what is ignored is the fact that some 20 years ago, people drank irrigation water without suffering jaundice epidemics. However, it is more convenient to lay the blame on the Ministry of Housing and Municipal Services. This department seems to serve as a lightning rod—everyone is perpetually complaining about it, but it complains perpetually as well: not enough resources, equipment and piping, not to mention the extremely disorganized army of sanitation engineers and yard-keepers. However, no matter how great the "contribution" of municipal workers to the spread of disease might be, this "contribution" has a bearing only on viral hepatitis A and other infectious diseases, while serum hepatitis is entirely on the conscience of the Ministry of Health.

(To be concluded)

Concern About AIDS in Uzbekistan

91/C0013B Tashkent PRADA LOSTOKA in Russian
29 Jul 90 p 3

[Article by Murad Mukhammad-Dost "Saffron Syndrome"; conclusion. See No 171 for the beginning]

[Text] A little information about AIDS. There was no such thing in Uzbekistan until recently. There was a kind of "semi-AIDS" discovered by R. Agzamov, deputy director of the Uzbek SSR Ministry of Health's Tuberculosis Institute. While examining patients from cotton-growing areas he established a weak immune system in 50 or more percent of them. He gave a report on this subject to the participants of a respected symposium. His presentation did not elicit any special alarm. The specialists were overwhelmed as it was by thoughts of real AIDS, which I repeat, was not yet encountered in Uzbekistan. The time to raise the alarm came when three infected individuals were revealed among the republic's inhabitants. As we know, AIDS is transmitted, besides by sexual behavior, by the same pathway as serum hepatitis—through dirty medical instruments, be they syringes in the hands of a nurse or forceps in the hands of a stomatologist. In this regard, AIDS and hepatitis B are blood brothers, so to speak. In the meantime the frequency of serum hepatitis infection is increasing. In 1989, for example, 43,353 persons suffered jaundice as a result of subcutaneous injections of medicines, intravenous infusions, etc. For comparison, 7,974 persons had the disease in 1979. It might be noted that during the years of stagnation, statistics were far from complete and undesirable facts were often left out of the records. This is so. But cover-ups are still encountered in our times of perestroika. Take, for example, a decision of the republic epidemiological council dated 29 September 1988—an official document stating where cases were supposedly not strictly reported, how often and in what circumstances. In the city of Shirin, the rate of concealment was 69.3 percent. Statistical manipulations bear unique features in regard to hepatitis. A viral hepatitis B diagnosis is simply replaced by a diagnosis of hepatitis A on reporting form No 85. And there's less trouble for the doctor as a result. An ordinary intestinal infection is one thing, but one caused by a syringe used in hospital is another. Victims of the latter totaled 5,500 just in Tashkent in 1988, which was 43.3 percent of all cases of viral hepatitis (there were as many as 6,426 cases in 1989). Let's get back to the matter of responsibility. Have any medical workers been punished for causing the suffering of a patient, for disabling him, and sometimes even killing him? Or for concealing cases of infection in the hospital, for forging diagnoses, or for misleading the public with false reports? The republic's Supreme Court confirmed what we already know as it is: Not a single court sentence was passed in a case involving viral hepatitis infection. And although criminal proceedings have been instituted in such matters, they were dismissed due to the absence of corpus delicti. The Uzbek SSR Criminal Code foresees only an article for "premeditated actions" by medical personnel. And what sort of

"premeditation" is there in a dirty syringe? This is why punishments are limited to reprimands, censures and other such "actions." Nothing more. Just between you and me, let me tell you about a person whose story might provide a little comfort. There lives and works a man by the name of Adkham Rasulev in Tashkent. Until recently he was reputed among medical officials as being a terrible intriguer, since he incessantly wrote letters to all levels of authority, appealing to their conscience. Yes, he believed, and still believes, that serum hepatitis infections occur not so much due to poor availability of medical equipment as due to a lack of conscience among medical personnel. This conviction was the product of many years of experience working as the chief physician of a clinic in the Institute of Infectious Diseases, and of a practical perception of the problem. It was before AIDS had become "a legacy of bourgeois society" that epidemiologist Rasulev decided, contrary to instructions of the USSR Ministry of Health, to subject all 100 percent of syringes to the amidopyrine test, rather than the recommended 1 - 2 percent (the amidopyrine test makes it possible to check the cleanliness of instruments, and serves as an indicator of their sterility). And so, his experiment revealed that traces of blood remain on 12 - 15 out of 100 syringes. Not being all that surprised by this, Rasulev went further. Immediately after some injections he put a batch of syringes aside while meticulously washing another. Once again the sterility test. The test results were the same in the first batch, while they were better in the second, although traces of blood still remained on 5 - 6 percent. In this way, he developed a simple procedure for processing dirty syringes step by step. Adhering to the simple tested rules, in 1981 - 1982, workers of Rasulev's clinic did not allow a single serum hepatitis infection within the hospital. And so, what happened? Rasulev's procedure failed to win over the hearts of functionaries at the Ministry of Health. They even reproached him for submitting a procedure that had nothing "innovative" about it (he never claimed it did, actually). And because he persisted, he was dismissed. His dismissal order was, of course, superseded later on by transfer to Clinical Tuberculosis Hospital No 1 where Rasulev once again engaged in "guerrilla warfare" at his own peril. Even work with a contingent of patients in an especially high risk group (many chronic alcoholics and drug addicts, the influx of homeless in the winter months, and dozens of carriers of B antigen) produced the same results. Not one case of serum hepatitis! Rasulev's colleagues began visiting him—some secretly, some openly. He soon acquired a group of allies who took it upon themselves to learn how to avoid infecting patients not only with viral hepatitis but also with all other diseases, including AIDS. Ultimately, it seemed that even the republic's Ministry of Health came to recognize Rasulev's unique "school" as something good. Even so, the matter ended with that. The Ministry of Health does not have the finances to support 100 percent amidopyrine testing at the scale of the republic as a whole. With this, it is said, Doctor Rasulev's patience ran out, and he exploded. Last year Rasulev was supported by about a dozen therapeutic institutions.

This year, beginning in January, his procedure was introduced in four of Tashkent's rayons. The results are clear: The number of cases of serum hepatitis in these rayons decreased by almost a factor of four. What would 100 percent sterility testing cost? Around 30,000 rubles a year. Generally not a small sum, but let's compare it with the cost of treating one hepatitis patient: 740 rubles with virus A, and twice more with virus B. In the meantime the republic spent 1,612,000,000 rubles to fight saffron disease in the 11th Five-Year Plan. Much more than the annual budget of all Uzbek medicine, including not only the treatment and feeding of patients but also acquisition of medical equipment, construction and so on. And what amounts came out of the trade union coffers to pay for temporary incapacitation of patients? And how much went to disability pensions? How much, then, do you think this saffron disease, which has ceased being the exotic disease it was in ancient times, costs the state and the citizens of our republic? Understandably, Doctor Rasulev's procedure cannot solve the hepatitis problem completely. It is one of the means of tangibly improving the state of affairs. And is this really very much to pay for such a possibility, considering the acute shortage of disposable instruments, considering the impending threat of AIDS, and most importantly, considering that human suffering does not yield to measurement, and every life is priceless? It was suggested at the 22nd Congress of Uzbekistan communists that "... public health cannot develop just on the basis of budgeted assets alone. It is very important to resolve the matter of creating a public health development fund soon, one which could receive assets from highly profitable enterprises, businesses, cooperatives and public organizations." It seems to me that something like a public health fund (we could name it after the great Avicenna) would receive real support.

Malignant Melanoma Incidence in Moscow

91TC00214 Leningrad VOPROSY ONKOLOGII in Russian Vol 36 No 6, Jun 90 (manuscript received 26 Jun 89) pp 611-615

[Article by T. S. Sitnikova, R. F. Garkavtseva, and I. V. Demidov, All-Union Oncology Scientific Center, USSR Academy of Medical Sciences, Moscow]

UDC 616.5-006.81:615.036.2

[Abstract] The incidence and prevalence of skin melanoma in Moscow were analyzed employing data from 1983 through 1987, encompassing 1,604 cases (521 in men and 1,083 in women) of the disease in people over the age of fifteen. For women aged 15 - 24 years, the risk is minimal, but then steadily increases and peaks at 40 - 44 years (37.58 cases per 100,000), with a second peak at 60 - 69 years (42 - 51 cases per 100,000). The incidence of skin melanoma in men exhibited peaks at 45 - 49 and 65 - 69 years. The results demonstrate that the incidence of skin melanoma increases with age and is higher among women aged 25 - 54 years. The findings also suggest that

there are several etiologically heterogenous forms of skin melanoma. Figures 1; tables 3; references 8: 3 Russian, 5 Western

Identification of *Borrelia* Isolated in USSR and Czechoslovakia From *Ixodes ricinus* Ticks

91TC0035B Moscow ZHURNAL MIKROBIOLOGII, EDDI MILOGII I IMMUNOBIOLOGII in Russian No 6, Jun 90 (manuscript received 23 Jun 89) pp 10-13

[Article by V. M. Kryuchevnikov, E. I. Korenberg, S. V. Shcherbakov, N. B. Gorelova, Z. Yurzhitsova, Yu. Galouzka, Z. Gubalek, Yu. V. Kovalevskiy, M. L. Levin and I. A. Bunikis, Scientific Research Institute of Epidemiology and Microbiology imeni N. F. Gamaleya, USSR Academy of Medical Sciences, Moscow; Institute of Systematic and Ecologic Biology, Czechoslovak Academy, Brno; Interdepartmental Scientific Research Laboratory of Regional Infections, Vilnius University]

UDC 579.834.114.083.18:595.42-167(437+[47+57])

[Abstract] *Borrelia* isolates from *Ixodes ricinus* ticks collected in 1988 in the Leningrad Oblast, Lithuania, and Southern Moravia in Czechoslovakia were subjected to serologic studies to assess the potential risk of Lyme disease. The study with monoclonal antibodies revealed seven strains of *Borrelia burgdorferi*, serotype II. These findings demonstrated that *I. ricinus* serves as a vector of *B. burgdorferi* in the USSR and Czechoslovakia and, accordingly, poses a threat in the spread of Lyme disease. Tables 2; references 21: 8 Russian, 13 Western

Ornithosis Outbreak at Textile Plant

91TC0035D Moscow ZHURNAL MIKROBIOLOGII, EDDI MILOGII I IMMUNOBIOLOGII in Russian No 6, Jun 90 (manuscript received 15 Jul 88, in final form 24 Nov 89) pp 39-43

[Article by Yu. Ya. Vengerov, Yu. M. Fedorov, A. A. Ivanov, I. A. Abramova, I. A. Kaganovich, O. A. Timasheva, V. P. Popov, A. A. Kardubaylov and I. M. Terskikh, Moscow Medical Stomatological Institute imeni N. A. Semashko, Main Administration of Quarantinable Infections, USSR Ministry of Health]

UDC 616.98.578.826.1]-036.22-057:677.024

[Abstract] An outbreak of ornithosis was recorded at a textile plant in December 1985 - January 1986, which affected 98 workers (20 males, 78 females, age range 16 - 64 years.) Diagnosis was based on epidemiologic, clinical and serologic grounds, with the infection traced to aerosol contamination with pigeon droppings. The clinical manifestations were typical and successfully managed with a tetracycline regimen, with no sequelae noted after ca. 1.5 years. Specific antibodies generally appeared after 3 - 67 days, with early antibiotic administration limiting the rise in complement fixation and passive hemagglutination titers. Figures 1; tables 4

Human T-Cell Leukemia Virus Type I (HTLV-I) Antibody Screening in Sera of Adult Population in Some Regions of USSR

917C00984 Moscow VOPROSY VIRUSOLOGII in Russian Vol 35 No 4, Jul-Aug 90 (manuscript received 11 Oct 89) pp 309-312

[Article by N. B. Senyuta, L. S. Yakovleva, V. N. Stepina, L. N. Buachidze, Ye. P. Gurova, Z. A. Kolodnitskaya, V. M. Kindyakov, and V. E. Gurtsevich, All-Union Oncological Scientific Center, USSR Academy of Medical Sciences, Moscow]

UDC 616.153.96-097:578.828.6]-078.833

[Abstract] The results of serologic investigation for human t-cell leukemia virus type I (HTLV-I) antibodies encompassing 4,118 serum specimens collected from healthy people of more than 30 nationalities and 55 residential areas of Khabarovsk and Primorsk Krays, Sakhalin Oblast, and Kamchatka are summarized. Also included are data on 1,037 blood donor samples from three blood donating stations in Moscow, South Sakhalinsk, and Komsomolsk-on-Amur. The serum samples, collected in 1986 - 1987, were obtained from persons aged 16 - 82 who had resided in the area for more than 20 years. Two cell lines MT-2 (HTLV-I⁺) and MOLT-4 (HTLV-I⁻) were used in passive agglutination of gelatin particles covered with virus proteins in conjunction with "Serodia ATLA" diagnostic kits. Overall, 75 persons (1.82 percent) tested positive for HTLV-I, which is much lower than the rate among healthy people in endemic areas (35 - 45 percent), but higher than the rate among those in European countries (less than 1 percent). The results demonstrated that HTLV-I was detected twice as often among the Nivkhi and Negidalets people, with inhabitants of Noglik on Sakhalin Island exhibiting a 6.4 percent rate of HTLV-I infection. In addition, women were shown to be twice as likely as men to test positive for HTLV-I. Early marriages and sexual contact at a young age are a possible explanation for the greater prevalence of HTLV-I among young people. Finally, the high rate of infection attests to the need for greater serological screening among the healthy population. Tables 2; references 18: 1 Russian, 17 Western.

Plague in Aral Region

91WE0093W Alma-Ata KAZAKHSTANSKAYA PRAVDA in Russian 18 Sep 90 p 1

[Article by KazTAG correspondent K. Imanberdiyev]

[Text] Aralsk (Kzyl-Orda Oblast), 17 September—Yet another misfortune has befallen this city of ecological disaster—the plague

I. Orynbasarov, a crane operator at a freight-handling equipment plant, was taken to the rayon hospital with a diagnosis of upper respiratory disease. The patient's state soon worsened drastically, and on 13 September he died. On that same day, Zh. Zhansugurov and T. Kadyrkulov were admitted to the hospital with high temperatures. It turned out that they and Orynbasarov had slaughtered a camel. Bacteriological tests were positive for the plague microbe.

Emergency epidemic-control commissions were quickly created in the Aralsk Rayon and oblast. A quarantine prohibited anyone's departure from Aralsk. All persons who had been in contact with Orynbasarov, Zhansugurov and Kadyrkulov were identified and isolated (except for one). A temporary hospital and other medical facilities were also opened.

The situation in Aralsk remains complex. Progress in fighting the epidemic is examined daily at a meeting of the oblast epidemic control commission, which is headed by oblast executive committee first deputy chairman A. K. Ibrayev.

Outbreak of Plague in Uzbekistan 'Localized'

917C01414 Moscow PRAVDA in English 14 Nov 90 Second Edition p 6

[UZTAG-TASS report: "Plague Infection Localized"]

[Text] An outbreak of plague has been localized as a result of emergency measures taken by doctors.

On the night of 6 November a well driller died in Bukhara Oblast hospital. Doctors determined the cause of death—a septic form of plague, complicated by pneumonia. It was established that the victim had been sinking wells near the central farmstead on the "Avangard" sovkhoz, in Uchkudukskiy Rayon. There was a serious epizootic of plague among the rodent population there. Rodent fleas had gotten onto a cat that lived in the caravan where the worker was living. It was a fleabite that led to the tragedy.

More than 30 people who had been in contact with the patient were isolated. Preventive treatment was administered and they are all well, 19 of them having even been discharged from hospital. Doctors are keeping all those living in the area of the epidemic under observation. They have been given prophylactic inoculation. The area has been disinfected and the rodents which carry the infection are being destroyed. Hunting of foxes, hares, jackals, wolves, and rodents has been banned in affected areas.

The plague outbreak has been localized, but doctors are on the alert—you don't trifle with plague.

Cytogenetic Sequelae of Wide-Band Noise

917C0129A Moscow GIGIYENA TRUDA I
PROFESSIONAL'NYYE ZABOLEVANIYA in Russian
No 9, 90 (manuscript received 28 Feb 90) pp 6-8

[Article by O. I. Timchenko, Ye. N. Shantyr, Ye. N. Antipenko and N. M. Paranko, Ukrainian Scientific Hygienic Center, Ukrainian SSR Ministry of Health, Kiev]

UDC 616-018.1-092.9-02:613.644]-07

[Abstract] Cytogenetic sequelae of exposure to wide-band noise were assessed in 3- to 4-month-old male and female Wistar rats. The animals were exposed to 40 12,000 Hz noise with intensities ranging from 80 - 100 dB for 4 h per days for 15 - 120 days. Examination of hepatocytes 30 h after partial hepatectomy demonstrated that a 15 day exposure was innocuous, while exposure to 100 dB for 3 months or to 90 dB for 4 months actually reduced the number of aberrant cells 1.3- to 1.4-fold. There were no changes in bone marrow cells. Exposure of male rats to 100 dB noise for 4 months, however, led to a 1.7-fold increase in the number of hepatocytes with chromosomal abnormalities. Consequently, these findings indicate that prolonged exposure periods are required for evaluation of the genetic sequelae of broad-band noise. Tables 3; references 11; 10 Russian, 1 Western.

Effects of Elevated Ambient Temperatures on Myocardium: Clinical and Experimental Studies

917C0129B Moscow GIGIYENA TRUDA I
PROFESSIONAL'NYYE ZABOLEVANIYA in Russian
No 9, 90 (manuscript received 22 Nov 89) pp 24-27

[Article by L. I. Bilyk, T. P. Kostenko and I. L. Filipchenko, Institute of Hygiene and Occupational Diseases, Krivoy Rog]

UDC 616.127-02:613.646]-07

[Abstract] The health effects of high ambient temperatures were assessed on a cohort of 1,255 workers exposed at a metallurgical plant, as well as on 1,028 workers employed under less adverse conditions from the temperature standpoint. EKG monitoring in conjunction with determinations of urinary levels of catecholamines, dopamine and DOPA, as well as blood chemistries for

lactate dehydrogenase (LDH) and creatine phosphokinase (CPK) revealed the cardiological health risk of high temperatures. In the former group, the incidence of abnormal EKG readings was 54.4 percent higher than in the control group, indication of ischemic heart disease was 2.7-fold greater, and incidence of left ventricular hypertrophy was 1.8-fold greater. These changes were accompanied by statistically significant elevations in blood levels of LDH and CPK—reflective of myocardial damage—as well as by changes in catecholamines, dopamine and DOPA suggestive of stressed adrenergic mechanisms. Elevations of LDH and CPK were found to be among the early indications of myocardial damage and, thus, suitable as markers in health monitoring. In addition, studies on outbred, 180 - 220 g, male rats subjected to 40°C for 4 h per day for up to 4 months in combination with a relative humidity of 50 - 60 percent provided histological confirmation of heart damage resulting from heat. References 10; Russian

All-Union Seminar of Young Scientists and Specialists on "Novel Biomolecular Aspects of Occupational Pathology, Toxicology and Hygiene"

917C0129C Moscow GIGIYENA TRUDA I
PROFESSIONAL'NYYE ZABOLEVANIYA in Russian
No 9, 90 p 60

[Article by L. M. Komleva and V. V. Ivanov, Institute of Labor Hygiene and Occupational Diseases, USSR Academy of Medical Sciences, Moscow]

UDC 616-057+613.6]:061.3(47+57)"1989"

[Abstract] The above conference was held on December 4 - 12, 1989 in Krasnoyarsk with the participation of leading specialists from 15 institutions and academic departments in Kiev, Moscow, Volgograd, Novokuznetsk, Tashkent and other major centers. A wide variety of topics pertaining to industrial pathology, toxicology, and hygiene were covered, including health ecology (V. V. Ivanov, Moscow), immunology and molecular pathology of the hepatobiliary system (Yu. P. Gichev, Novosibirsk), cytochrome P-450 as a bioindicator (V. M. Mishin, Novosibirsk), and mitochondria in toxicity testing (G. G. Avilova, Moscow). Other major topics dealt with secondary messengers (N. A. Fedorov, Moscow), cell structures in screening studies (R. A. Ryazanov, Moscow), and endocrine-epithelial interactions (V. V. Yaglov, Moscow).

Individual Stereotypes of Human Neuropsychic Prognostic Activity in Problem Situations With Different Probability Structures

917C0045 Riga IZVESTIY VEŠEYSHKOY
AKADEMIY NAUK in English No 9, Sep 90 pp 86-96

[Article by A. Krauklis and I. Kazanovskaya, Research Institute of Experimental and Clinical Medicine]

UDC 612.821

[Text] The formation of man's adaptive psychophysiological reactions, their individual variants and different degrees of adaptive effectiveness in problem situations were studied by a decision-making model. It was established that the form of manifestation depends on the probability structure of the problem situation. Every subject displayed substantial difference in individual speed in forming an adequate pattern of action after a stereotype signal sequence, with motor automation preceding detection of the stereotype signal sequence. On the basis of the time required by the subjects to detect the stereotype presentation of signals, the dynamics of the problem-solving time and the intensity of effector reactions, individual variants of neuropsychic self-regulation stereotypes characterized by differing adaptive effectiveness were revealed.

Introduction

Increasing importance attaches today, in the context of the extensive scientific problem of man's adaptation to environmental conditions, to factors connected with the specifics of a large number of professions in which information processes play a leading role. The intensive load on sensor systems, in particular that of sight, and the high intellectual and emotional stress placed on operators dictate the urgent practical necessity for a comprehensive study of the adaptive reactions of the brain connected with the perception, registering and processing of visual information to provide for the higher forms of analytic and synthetic activity.

There is a hypothesis according to which man functions as a single channel with limited capacity [1-2], so that if this capacity is exceeded, overloading of the nervous system is the result [2-5]. It was a conception leading to a number of studies into man's capability of processing information with varying quantity, complexity, intensity, newness, uncertainty and significance of the signals received. It thus happens that the object of most exhaustive study in the operational structure of human information processing is the primary sensor component [6-11], whereas central components such as the forms of problem solving and reaction stereotypes have been considerably less studied.

There has been extremely little study in the aspect of individual variants of human neuropsychic prognostic activity and of the elaboration of individual stereotypes for overcoming excessive stimulus loads.

The present paper is based on the view that the problem of enhancing the reliability of man's activity in information systems can be solved by revealing and bringing into action his or her brain's self-regulating capability, which would permit optimizing measures to be coordinated with individual peculiarities of neuropsychic self-regulating mechanisms and optimal use to be made of the brain's functional resources.

Methods

In laboratory conditions a situation was modelled in which the subjects solved logical problems of classifying two-digit numbers, the time for solving the problem being successively decreased, work resembling that of an operator decoding incoming information. The method was worked out in the form of a program for a digital electronic computer (DEC).

Subjects: 21 healthy students (having normal or corrected eyesight) aged 19 - 29 took part in 231 experiments.

Stimuli and Procedure: Two digit numbers were displayed in succession on the screen of a DEC at the control panel where the subject sat. Each number was displayed for 1 s. According to the instructions, the subject was required to determine, by the rules given in Table 1, to which of eight possible classes the numbers belonged, and to depress the corresponding class number on the keyboard of the computer.

Table 1. Algorithm for Decoding Numbers

Digit number	Class
I greater than II*	first
I less than II	second
I greater than -II	third
I less than -II	fourth
I greater than II	fifth
I less than II	sixth
I greater than -II	seventh
I less than -II	eighth

*I—the first. II—the second.

For example—"If the first digit number is less than the second one, these numbers belong to the second class" or "if the first digit number is more than the second one and its sign is minus, these numbers belong to the fifth class" etc.

The subject was not told that the pairs of numbers corresponding to a definite class might follow one another in a strictly stereotypical or random sequence in the batch of numbers. When the display of the second number ended, a masking stimulus appeared on the screen, whereupon the meter of the check classification time was switched on for 6, 4, or 1 s for these different experimental series. When the subject had registered his or her answer, an evaluation of his or her reaction

appeared on the screen: 5—for the correct solution, 2—in the event of a mistake or late solution. During the time (2 s) the evaluation was displayed, the subject had to free the keyboard of the class number by depressing the release key. Delay in doing this and the length of the delay were recorded in the DEC memory block. The keyboard releasing reaction corresponds in time to achievement of readiness to receive the next signal.

At each series the subject was shown 90 - 100 pairs of numbers in a total program time of 10 - 15 minutes.

To begin with, a batch of numbers containing 2 classes was presented and the classification time was 6, 4 and 1 s. In the following stage of the study, the subject worked with a batch of numbers containing 4, then 6, and finally 8 classes, the check classification time being also 6, 4, and 1 s. In all the programs enumerated, the classes followed in strict stereotype sequence, (e.g. I, II, I, II and so on, for a sequence containing two classes, and I, II, III, IV, I, II and so on, for a sequence containing four classes). The instructions given to the subject did not reveal the sequence of the signals.

After completion of these programs, a batch of numbers was presented containing 8 classes in random sequence and also with 3 time regimes.

When the experiment was over, the data printer recorded the dynamics of mistakes made, delay in freeing the keyboard, "time of lagging" (seconds), number of mistakes, and problem-solving time (milliseconds). The moment when each subject detected the stereotype sequence of signals was also recorded.

To characterize the subjects' physiological reactions and analyse their trend, a polygraphic recording of the ECG in standard II derivation for a heart-rate count and pneumogram for analysis of breathing frequency was made by a polygraphic recording and attachments before the study, during the whole duration of the test period and for 5 - 8 minutes of the post-period.

The experimental material was statistically processed using nonparametric tests.

Results

Analysis of the subjects' activity in classifying the numbers showed that the average "time of lagging" and number of mistakes with stereotype presentation (p less than 0.01): 9.8 \pm 1.4 and 16.0 \pm 3.1 mistakes respectively (6 s regime for classification), 5.5 \pm 1.3 mistakes and 7.0 \pm 1.9 mistakes (4 s regime), 4.0 \pm 1.2 and 8.0 \pm 0.1 mistakes (1 s regime); 16.0 \pm 3.1 ms and 10.9 \pm 2.7 ms "time of lagging" (6 s regime), 4.0 \pm 0.3 ms and 6.4 \pm 1.3 ms (4 s regime) and 1.4 \pm 0.6 and 2.4 \pm 0.4 ms (1 s regime). Analysis of the recorded physiological indicators showed also less tension of the vegetative processes with stereotype presentation (p less than 0.05) for heart contraction frequency and (p less than 0.01) for breathing frequency.

When the test program was carried out with stereotype signal presentation, each successive increase in the number of new classes in batch of digits to be analyzed was accompanied by a temporary lowering of the problem-solving effectiveness indicators and a rise in the activity of the vegetative nervous system. Adaptation to a new program is relatively quick, and when studies are repeated, even with more rigid time regimes for classification, a lowering of the number of mistakes and of the "time of lagging" is observed (p less than 0.05). As the information load (number of new classes) is increased, the time regime begins to play a greater and greater role, and in the 1 s regime for classification of signals a secondary mistakes peak is observed.

In analyzing the causes leading to the appearance of two mistakes peaks (6 s and 1 s), the first phase in information processing (sensor memory) should apparently be excluded as a possible source of mistakes. This can be justified by the fact that the reception and preperception storing of visual information is done in 10 to 160 ms [6, 7, 12], and in our conditions each number was displayed for 1000 ms. The considerable number of mistakes made during this time may be due rather to the subjects' superficial mastering of the decoding algorithm which is corroborated by the quick lowering of the number of mistakes when the experiments are repeated.

With the pattern in which the experiment was carried out, the subjects' activity was cyclical comprising the following stages: reception of the information, solution of the problem, motor reaction, check by feedback, release of the keyboard. The cycle was then repeated. The increase in the amount of information, due to a new task added to what had already been mastered, probably did not allow the functional brain condition to be achieved in time corresponding to readiness to receive a signal. It may be assumed that in the conditions of work described, the self-regulation of the problem-solving mechanism was effected by decreasing the volume of information perceived, omitting some decoding reactions and increasing the time necessary for its processing and integration, thereby lowering the "information per time unit" indicator. Presumably the duration of all the processing stages was increased, but owing to the specifics of the method employed, this was more noticeable during the final phase of the cycle, i.e., release of the keyboard which apparently corresponds in time to readiness to receive the next signal.

The second peak of mistakes (1 s regime) can presumably be explained proceeding from the hypothesis that man functions as a system with limited capacity [2, 6], therefore the processing of a second signal may in many cases be delayed if the first signal is still being processed [12]. The term "psychological refractory period" is generally accepted to designate analogous phenomena. The distinct increase in the number of mistakes in the 1 s regime may be evidence that this time regime itself introduces certain central limitations of the problem-solving process according to a present algorithm. In this same regime, there is a secondary rise of emotional tension (a

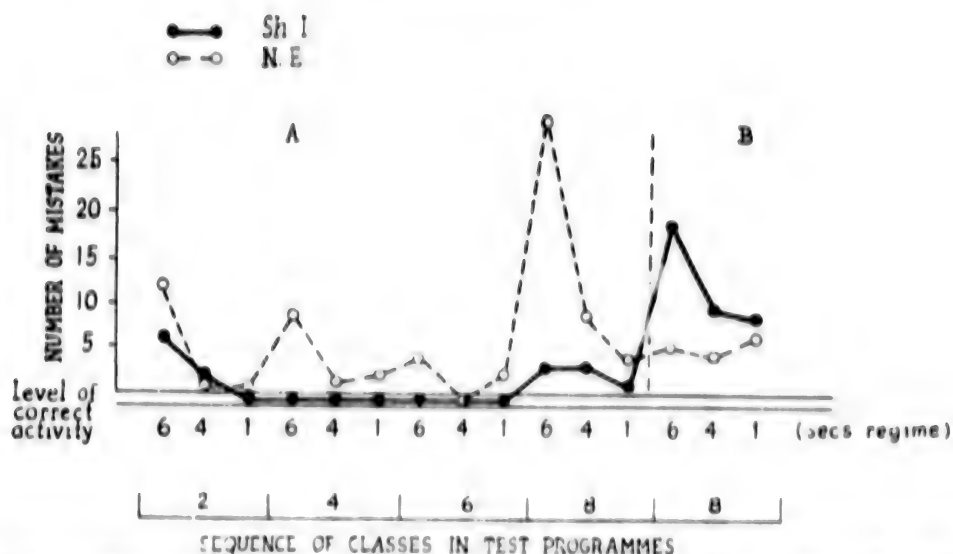


Figure 1. The number of mistakes in classifying signals presented in stereotype (A) and random (B) sequence by subjects Sh.I. and N.E. characterized by shorter and longer time to detect the stereotype. (The signs— and— show the programs in which the subjects detect the stereotype in signal presentation)

considerable increase of breathing frequency during the test period and maintenance of high level during the following post-period), resulting from the increased demands in the problem-solving phase.

The experimental data testify that during the fulfillment of the first part of the study, characterized by strict succession in signal presentation, the subjects realize relatively late the presence of a stereotype in the signal presentation; the moment of realization varied within the wide range of 100 - 500 pairs of numbers presented. Following the realization of the stereotype a decrease was noted in all subjects both in the number of mistakes (from 8.0 ± 1.5 to 3.3 ± 0.6 , p less than 0.01) and in the "time of lagging" (from 15.4 ± 2.8 to 5.5 ± 1.3 ms, p less than 0.01), as well as a drop in heart rate and breathing frequencies. During fulfillment of the next classification, problem heart and breathing frequencies increased by 4.7 percent and 11.5 percent respectively.

Table 2. Problem-Solving Time of Subjects Characterised by Quick Detection of the Stereotype of Sequence of Classes in a Program When Classifying a Batch of Digits of Increasing Complexity

Classes	Average problem solution time, in ms	
	Subject S.L.	Subject P.A.
2	2330	3150(?)
4	4740	1650
6	2340	1960
8	1560(?)	2020
8 (in random sequence)	2930	5940

In some cases the realization is preceded by motor automatism. This fact was corroborated also by the data for the average problem-solving time. In a separate series of the study, an additional experiment was carried out with each subject before the main one to reveal for each one of them the optimal display time of four-digit numbers which they had to classify according to an algorithm similar to the one mentioned above, comparing the first two and last two digits. Simultaneously, the average time for the simple motor reaction on the DEC keyboard was determined. Subtraction of the duration of the motor reaction (efferent motor component) from the total time gave the time spent on central processing of the information—solving the problem.

Table 2 shows the average problem-solving time for subjects characterized by quick detection of the stereotype.

It follows from the Table data that subject S.L. (who was slower to identify the stereotype) showed a sharp decrease of the problem-solving time (from 4740 ms to 2340 ms) in classifying the batch of numbers containing 6 classes. S.L. had not yet detected the stereotype signal sequence in this program. The achievement of motor automation was accompanied by a 216 - 780 ms decrease in the problem-solving for the group.

Subjects who noticed the stereotype quickly were far less successful in classifying signals presented at random sequence: They showed a sharp increase in the number of mistakes and the time of lagging (Fig. 1, 2) (p less than 0.01) compared with subjects who were slower to detect the stereotype. There were similar changes in breathing and heart contraction frequency indicators during solution of problems with random signal sequence in the case

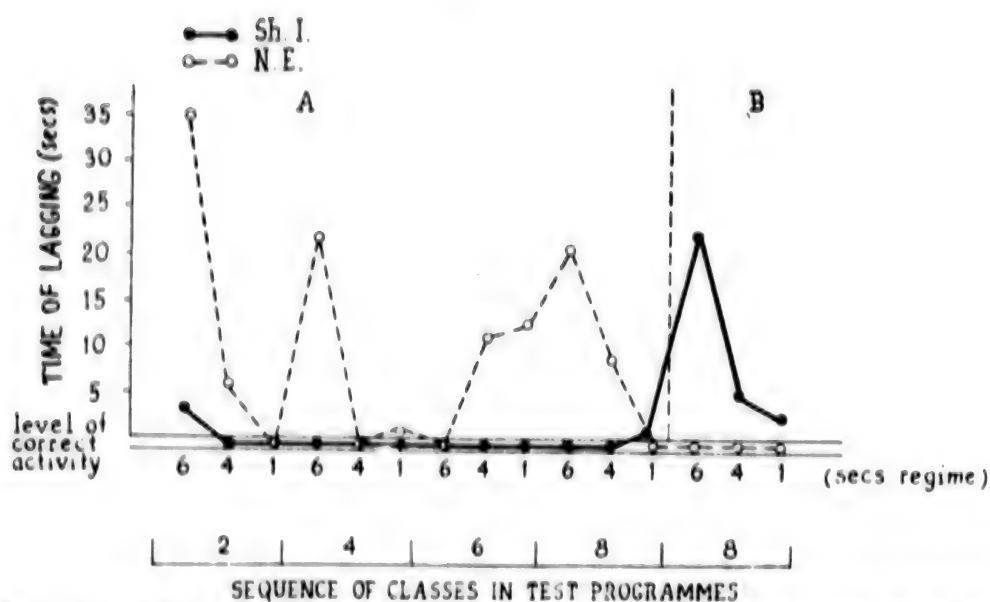


Figure 2. Comparison of "time of lagging" in subjects Sh.I. and N.E. characterized by shorter and longer time to detect the stereotype. (Conventional signs are the same as in Figure 1.)

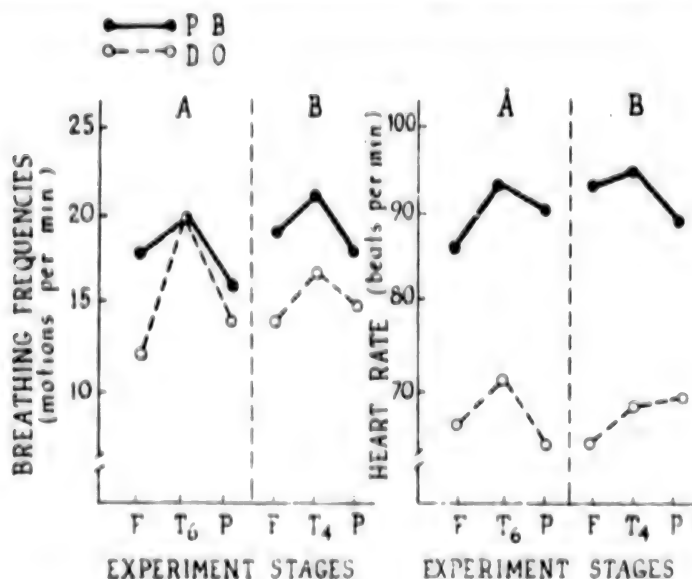


Figure 3. Heart-rate and breathing frequency changes in subjects P.B. who detected the stereotype in 6 s regime of signal presentation (A—before detection, B—after detection) and D.C. who detected the stereotype in the 4 s regime. (F—foreperiod; T₆, T₄, T₁—test periods; P—post period)

of subjects characterized by early detection of the stereotypical signal sequence: Heart rate, and breathing frequencies considerably exceeded the corresponding indicators for subjects who were slower to detect the stereotype (p less than 0.05; p less than 0.01).

As shown in Figure 3, breathing frequency of subject P.B. during problem-solving (classification of numbers

belonging to 6 classes with the 6 s classification regime) increased from 12 respiratory motions per minute at the beginning to 20 at the time of problem-solving, i.e. an increase of 66 percent. Heart contraction frequency rose correspondingly from 66 contractions per minute in the initial condition to 71 during problem-solving time (an 8 percent increase).

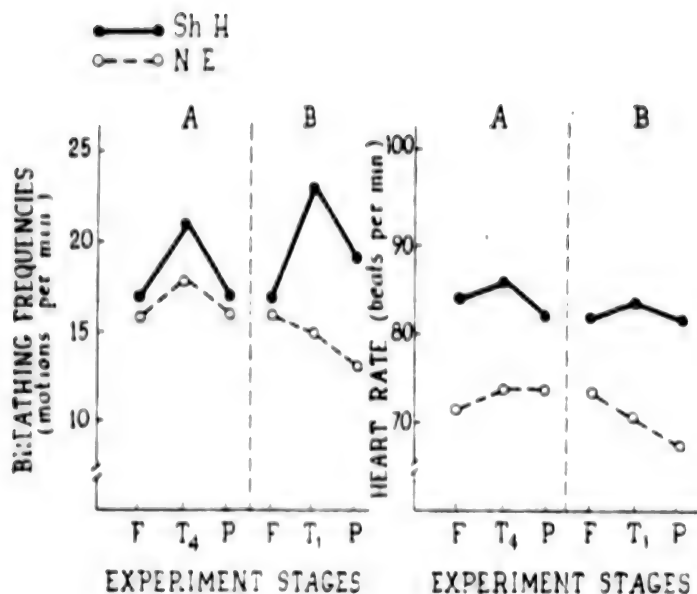


Figure 4. Heart-rate and breathing frequency changes in subjects Sh.H. who detected the stereotype in 4 s regime of signal presentation and N.E. who detected the stereotype in 1 s regime.
(Conventional signs are the same as in Figure 3.)

After realization of the stereotype signal presentation (which occurred during the solving of the problem mentioned, despite the time regime of the next problem being more complicated (4 s for classification), the changes in the breathing frequency of subject P.B. were less considerable, only 17 respiratory motions per minute (an increase of 21 percent). Heart contraction frequency reached only 68 per minute.

Figure 4 shows how the reaction of the vegetative nervous system of subject D.O. (who did not detect the stereotype signal sequence in the same conditions) differed from the above-cited data. D.O.'s transition to fulfillment of the following, more complicated programme was accompanied by the due rise in heart contraction and breathing frequencies. The differences revealed in the reaction of the vegetative nervous system of subjects who distinguished themselves by the time taken to detect the stereotype persist regardless which programme the subject is carrying out and in which regime at the moment of detection. Figure 4 presents also analogous data reflecting the differences in the structure of the vegetative nervous system's reaction in subject Sh.H (who had detected the signal presentation sequence) and subject N.E. for whom this feature of the programme still remained unknown.

Discussion

The results obtained show that the reliability and effectiveness of an operator's work in classifying digit symbols in a situation with a varying degree of uncertainty is conditioned by the achievement of adequate functioning regimes of the neuropsychic self-regulating mechanisms,

which ultimately ensure a level of information processing adequate to the given degree of uncertainty.

By the term neuropsychic self-regulation we mean a change in the functioning of the central nervous system towards integration of the behavioural, psychic and vegetative aspects of the organism's activity ensuring, along with adaptation of the organism to the external environment, the most adequate functioning level of the central nervous system itself [13-15]. Analogous is the meaning of the above-cited concept of a number of authors studying the mechanism of dynamic self-regulation of the central nervous system's adaptive activity in animal and man [16, 17].

In analysing the results obtained, attention is aroused by the considerable increase in the effectiveness of the work, accompanied by a change of the vegetative indicators (lower frequency of heart contraction, decreased breathing activity) throughout the whole group of subjects after they have detected the stereotype signal sequence.

Uncertainty of the situation in carrying out any activity is known to cause anxiety and emotional stress reactions, an objective indicator of which is an increased vegetative activity. In some works [18] uncertainty of the situation is considered as the main and even the universal emotion-producing factor. Thus, in a condition of emotional stress caused by uncertainty of the environment, there is activation of the neuropsychic self-regulation mechanisms directed at bringing the organisms energy and functional resources into action for the purpose of broadening the individual's adaptation capability and

ensuring an adequate functioning level of the nervous system during problem-solving.

Perceiving only the immediately presented external information on the first acquaintance with the rules of unfamiliar activity, as skills are acquired, the organism begins to single out as significant also the concealed characteristics of the environment, and this promotes the achievement of adequate self-instruction. Information on the structure of the environment, returning in the form of a corrective command [19], forms more precise specialised and adequate reactions—effector outlet. Thus, when the subject detects the stereotype signal sequence (adequately reflects the external environment), his/her subjective uncertainty of the situation is eliminated and the level of emotional stress resulting from it is lowered.

It must be noted that throughout the whole group studied, once the subjects had detected the stereotype signal sequence, the number of mistakes dropped. Judging by the subjects' own account they went on from solving the decoding problem to forecasting the following class number. The subjects' transition from the state of continual and global readiness to perceive signals to the level of forecasting each following class is apparently accompanied by a decrease in the flow of information, and this optimises the psychophysiological state of nervous activity, making it more economical.

It must be noted that in some cases conscious detection of the stereotype is preceded by unconscious motor automatism. This is corroborated both by the above-cited data on problem-solving time and by subject L.Sh.'s own account during work before detecting the stereotype: "I have a strange feeling that I depress the answer key before I have finished classifying—I act before I have found the solution..."

The results of the study also testify that an adequate subjective pattern of action with stereotype signal presentation is formed at different speeds by different subjects. Thus at the first stage of stereotype detection, the subjects unconsciously registered only the motor reaction sequence. After a while the motor component of the stereotype lost its autonomy and was consciously controlled, yet conscious registration of the sequence of (intellectual) operations required considerably more time.

These facts are explained to a certain degree by data [20] generalising the data of a number of researches and testifying that the duration of the mark storage in the motor memory is considerably longer than that of the storage in the visual memory.

Presumably the difference noted in the speed at which a subjective pattern of action was formed was due to individual peculiarities in the subjects' neuropsychic self-regulation, in particular to specific features in the functional structure and adaptive trend of the orienting and general perceptiveness reactions reproduced to overcome the uncertainty of problem situations. With one

group of subjects the uncertainty of the situation of the nerve structures and functional systems ensuring the subjects' readiness to react adequately to any unforeseen signal. With the other group this uncertainty is overcome by maintaining the activity of the nerve structures and functional systems ensuring the search for more simple and economical problem-solving algorithm than those suggested in the instruction, in particular with the search for the order of signal sequence.

The effectiveness of the work of the groups of subjects involved varied when they passed on to test problems with random signal presentation: subjects who detected quickly the stereotype of the class sequence in the first series were considerably less successful in coping with random signal presentation than those who were much slower to detect the stereotype signal sequence in the first series of studies.

Taking into account the circumstance that a problem situation with random signal presentation is characterised by strongly pronounced uncertainty, it may be assumed that in this regime adequate information processing requires considerably more intense activation of the brain's corresponding nerve structures than in the regime of stereotype signal presentation. An indirect corroboration of this is provided by the increased vegetative changes, which are non-specific indicators of tension. There is an increase also of the subjective feeling of alarm and emotional stress experienced by the subject.

It is known that complicated functioning conditions bring into action the individual's past experience, which reflects also the individual peculiarities of his/her nervous activity [13-15], whereby individual features of adaptation are connected, on the one hand, with evolutionally determined (genetic) mechanisms of his/her functional systems, which, according to the conception of N. Bekhtereva [1], belong to the rigid regulating links, and, on the other hand, with qualities acquired individually in the process of vital activity and through which the flexible forms of interaction with the environment are ensured.

It is probable that the definite limitation which our study has revealed in the capability of the brain of a certain number of subjects to establish and maintain an optimal functional condition in a problem situation characterized by pronounced uncertainty, is determined not so much by the brain's lack of energy and functional resources as by neuropsychic self-regulation stereotypes evolved and consolidated by the individual's life experience and expressed in a timely (but partially inadequate) "saving up" of functional and energy resources by transition to a more economical regime of nervous activity—the quickest possible revelation of stereotype (order) in external events, and formation of stereotype response reactions. It may be presumed that in the group of subjects characterized by quick detection of the stereotype presentation of signals, quick formation of a definite dynamic stereotype is one of the principal conditions determining success of their activity in a

stereotype-organized environment. At the same time, the elaboration of determinate behaviour tactics is determined in them by a neuropsychic regulation stereotype so rigid that it exerts too much influence on current perception, when working in conditions of random organization of signal presentation, and deprives their activity of the necessary flexibility. In conditions of great uncertainty of the environment the nervous system of such subjects apparently required considerably more time to achieve the structure of activity corresponding to the conditions.

In subjects characterized by slower detection of the stereotype sequence of signals the achievement of an optimal functional conditions proceeds according to the type of stable activation of the neurodynamic processes which determine lasting readiness of the systems to perceive signals and bring the vegetative apparatus into action in a considerable degree. A more adequate regime of work for the brain of such subjects in a probability environment is apparently to refrain from arbitrary probability forecasting.

Thus, with subjects having a very marked inclination to probability forecasting, the pattern of events in the external world is more standardised and limited, still it ensures highly effective activity giving a problem structure adequate to these requirements. The pattern of events in the external world with subjects having a weakly marked inclination to probability forecasting is more indefinite, yet at the same time more labile, offering advantages for work in a situation with a more complicated probability structure. Presumably both types of neuropsychic self-regulation have their advantages, which can be manifested in the corresponding conditions of activity. The most advantageous situation will doubtless be that of the individual in whom both types of self-regulation are equally developed, their preferential employment being determined by the concrete problem situation.

Bibliography

1. Bekhtereva, N. P., "Neurofiziologicheskiye aspekty psikhicheskoy deyatel'nosti cheloveka," [Neurophysiological Aspects of Human Mental Activity], Leningrad, 1971.
2. Welford, A., "Stress and Performance," *ERGONOMICS*, Vol 16, No 5, 1973, pp 567-580.
3. Khananashvili, M. M., "Experimental Information Neuroses," *ZHURNAL VYSSHEY NERVNOY DEYATELNOSTI*, No 4, 1974, pp 175-182.
4. Khananashvili, M. M., "Informatsionnyye nevrozy," [Informational Neuroses], Leningrad: Meditsina, 1978.
5. Lipowski, L., "Sensory Overloads and Behavior," *PSYCHOTHERAPY A. PSYCHOSOMATIC*, Vol 23, No 1-6, 1974, pp 267-271.
6. Glezer, V. D. and Tsukkerman, I. I., "Informatsiya i zreniye," [Information and Vision], Leningrad: Nauka, 1961.
7. Glezer, V. D. and Nevskaya, A. A., "Ob odnovremennoy i posledovatel'noy obrabotke informatsii v zritel'noy sisteme," [Simultaneous and Sequential Information Processing in the Visual System], *DOKLADY AKADEMII NAUK SSSR*, Vol 155, 1964, pp 711-714.
8. Glezer, V. D., Dubkin, K. N., and Kuperman, A. M., "Zritel'noye opoznaniye i yego neyrofiziologicheskiye mekhanizmy," [Visual Perception and Its Neurophysiological Mechanisms], Leningrad: Nauka, 1975.
9. Haber, R. N., and Standing, L. G., "Direct Measures of Short-term Visual Storage," *QUART. EXP. PSYCHOL.*, Vol 21, 1969, pp 43-54.
10. Lindsey, P. and Norman, A. D., "Human Information Processing," New York: London: Academic Press, 1972.
11. Eriksen, C. W. and Spencer, T. L., "Rate of Information Processing in Visual Perception: Some Results and Methodological Considerations," *J. EXP. PSYCHOL. MONOGR.*, Vol 79, 1969, pp 1-16.
12. Sperling, G., "The Information Available in Brief Visual Presentations," *PSYCHOL. MONOGR.*, Vol 74, 1960, pp 1-29.
13. Krauklis, A. A., "Uslovno-reflektornaya regulatsiya nervnoy deyatel'nosti," [Conditional Reflex Regulation of Nervous Activity], Riga: Izdatelstvo AN LatvSSR, 1960.
14. Krauklis, A. A., "Samoregulatsiya vysshey nervnoy deyatel'nosti," [Self-regulation of Higher Nervous Activity], Riga: Izdatelstvo AN LatvSSR, 1964.
15. Krauklis, A., "Emocionalais stress un ta optimizacija," Riga: Zvaigzne, 1981.
16. Ivanov-Muromskiy, K. A., "Protsessy samoregulatsii kory golov'nogo mozga v razlichnykh funktsional'nykh sostoyaniyakh," [Self-regulatory Processes of the Brain Cortex in Various Functional States], Kiev: AN UkrSSR, 1974.
17. Zimkina, A. M., Menitskiy, D. N., Antomonov, Yu. G., Zingerman, A. M., et al., "Mechanisms of Self-regulation of Functions and Functional States," in "Adaptivnaya samoregulatsiya," [Adaptive Self-regulation], Moscow: Meditsina, 1977.
18. Simonov, P. V., "Emotsional'nyy mozg," [The Emotional Brain], Moscow: Nauka, 1981.
19. Anokhin, P. K., "Biologiya i neyrofiziologiya uslovnogo refleksa," [Biology and Neurophysiology of the Conditional Reflex], Moscow: Meditsina, 1968.
20. Haber, R. N., "Information Processing Approaches to Visual Perception," New York, 1969.

COPYRIGHT: Izdatelstvo "Zinatne". "Izvestiya Latvyskoy akademii nauk", 1990

Field Trials with Plasma Subunit Hepatitis B (PSHB) Vaccine

917C0035E Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian* No 6, Jun 90 (manuscript received 16 Jun 89) pp 53-58

[Article by V. N. Ikoyev, M. A. Gorbunov, V. A. Ananyev, A. A. Sumarokov, Sh. Sh. Shavakhabov and K. A. Khalitov, Institute of Standardization and Control of Medical Biological Preparations imeni L. A. Tarasevich, USSR Ministry of Health, Moscow]

UDC 615.371:578.891].028

[Abstract] Trials were conducted with a Soviet hepatitis B vaccine prepared from plasma samples of HBsAg carriers. The vaccine is inactivated by a formaldehyde-E-leucine mixture and adsorbed to aluminum hydroxide, containing 20 µg/ml of HBsAg. Studies on 500 3- to 5-year-old children in Fergana, Uzbekistan, demonstrated the efficacy of the vaccine in the prophylaxis of hepatitis B in the pediatric population. Complete protection was obtained with a schedule of 3 i.m. immunizations (0-1-6 mo) over an 18 month period, whereas in placebo-treated children the morbidity was 8.9/1000. Seroconversion to a positive status in the immunized children was on the order of 90 percent after the full schedule of immunization. In addition to its high efficacy, the vaccine was also shown to be essentially areacogenic. Tables 2; references 6: 2 Russian, 4 Western.

Postinfectious and Postvaccinal Anthrax Immunity in Humans

917C0035F Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian* No 6, Jun 90 (manuscript received 7 May 89) pp 71-76

[Article by V. A. Abalakin, Sh. S. Dzhabirov, V. A. Kalita, V. K. Kuttugulov, S. A. Amireyev, A. G. Knop and B. L. Cherkassiy, Central Scientific Research Institute of Epidemiology, USSR Ministry of Health, Moscow]

UDC 615.371:579.852.13].015.46.07

[Abstract] An analysis was conducted on the status of human postinfectious and postvaccinal anthrax immunity in Alma-Ata Oblast and Chimkent in order to better assess retrospective value of serologic monitoring. The results demonstrated that subjects who had sustained an infection maintained high antibody titers (> 1:250) against the protective antigen (PA) (75 percent of subjects) and the lethal factor (LF) (96 percent of subjects) for 6 years. In addition, in these subjects IgG anti-LF titers were much higher than IgM titers. Vaccination with live STI-1 vaccine led to antibody formation in 72 percent of the vaccinees in 2 - 7 months, with essentially equivalent IgG and IgM titers and somewhat greater anti-PA titers than anti-LF titers. However, after 1 - 2

years, only 21 percent of the vaccinees had detectable antibody levels. Figures 6; tables 3; references 14: 6 Russian, 8 Western.

Development of Acarid Antigen-Based Vaccines and Antisera for Prophylaxis of Tick-Borne Encephalitis (TBE)

917C0035H Moscow *ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian* No 6, Jun 90 (manuscript received 11 Jul 89) pp 103-109

[Article by V. I. Votyakov and N. P. Mishayeva, Belorussian Scientific Research Institute of Epidemiology and Microbiology, Minsk]

UDC 615.371:578.833.26].03.07

[Abstract] Animal trials have demonstrated that immunization with salivary antigens of ticks constitutes an effective means of preventing the spread and severity of TBE. Generation of such antibodies interferes with tick feeding and hence virus transmission. Albino mice immunized against acarid antigens of *Ixodes ricinus* or *Dermacentor andersoni* have a 46 - 61 percent greater survival rate, concomitantly with a marked reduction in viremia. In addition, immune status of animals has also been shown to affect feeding ticks. The feeding time of ticks on animals possessing anti-acarid antibodies is prolonged by 1.2- to 2-fold, the ticks show a 27.5 - 50.6 percent weight loss, the number of satiated ticks is reduced by 38.9 - 64.2 percent, and tick fertility is reduced. In other trials, immunization of animals with a combined viral-acarid antigen vaccine has been shown to result in complete inhibition of viral reproduction and dissemination. These findings indicate that induction of an immune response against the tick vectors of TBE or the use of immune sera for passive immunization may be an additional approach to TBE prophylaxis. Tables 3; references 14: 9 Russian, 5 Western.

Immunostimulant Properties of Ethylene Oxide and Propylene Oxide Block Copolymers (Poloxamers)

917C0099D Moscow *IMMUNOLOGIIYA in Russian* No 4, Jul-Aug 90 pp 76-79

[Article by I. N. Topchiyeva, S. G. Zavgorodnyy and S. V. Osipova, Institute of Immunology, USSR Ministry of Health, Moscow; Moscow State University imeni M. V. Lomonosov]

UDC 615.275.4:547.313.2/.3].015.46:612.017.1.063

[Abstract] (CBA x C57Bl/6) F₁ mice were injected intraperitoneally with sheep erythrocytes + poloxamers to assess the immunostimulant properties of the latter. The results—counts of antibody forming splenic cells 4 - 5 days later—demonstrated that 3000 D poloxamers with 40 percent polypropylene glycol were the most

efficient adjuvants and that their efficacy improved with an increase in the molecular weight. Hydrophilic polymers consisting of polyethylene glycol lacked adjuvant properties, while hydrophobic polyethylene glycol polymers were active. Introduction of hydroperoxide groups and polyelectrolyte fragments into the poloxamers had

no effect on the immune response but reduced the optimum poloxamer dose. Modification of the poloxamers with solubilizer Pr128 and cumyl hydroperoxide led to a 10-fold increase in antibody production without affecting the optimum adjuvant dose. Figures 5; tables 1; references 15: 7 Russian, 8 Western.

Laser Treatment of Heart Arrhythmia

917C00151 Leningrad *LENINGRADSKAYA PRAVDA*
in Russian 30 Aug 90 p 1

[Article by B. Samoylov; "Using Laser Instead of Pacemaker"]

[Abstract] Specialists from the Atomic Energy Institute imeni I. V. Kurchatov and the Cardiovascular Surgery Scientific Research Institute imeni A. N. Bakulev under the direction of Leonid Bokeriy have developed a technique of treating heart arrhythmia with a laser. The treatment, considered by specialists as a breakthrough in medicine, involves laser irradiation of the arrhythmic zone of the heart. The surgeon checks his movements by watching the monitors and continues the laser treatment until the electrocardiogram normalizes. With a pacemaker, the patient is restricted by a number of factors—weather, external electromagnetic fields, and accidental injury. In addition, the pacemaker needs to be replaced periodically. More than 40 such operations have been performed, with good results. Researchers are currently striving to improve this technique to the point that it will no longer be necessary to open the thoracic cavity to perform this surgery.

Safety Assessment of New Laser Devices

917C00224 Moscow *GIGIYENA TRUDA I
PROFESSIONAL'NOYE ZABOLEVANIYA* in Russian
No 6, Jun 90 (manuscript received 31 Jan 89) pp 32-35

[Article by L. I. Lipkina, A. V. Levina, A. A. Polynkova, and N. L. Tsirkova, Hygiene Institute imeni F. F. Erisman, Moscow]

UDC 613.648:615.849.1]-07

[Abstract] The safety of the Biryza gas laser devices was evaluated at various phases of design and encompassed tests of laser radiation, noise, vibration, and electromagnetic field levels. The Biryza, with 1 kW of power, was tested on metallic and nonmetallic materials with varying thicknesses. Included in the investigation of the laser radiation reflection levels were tests on the optic and thermal properties of the material, surface condition, and cutting speed. The Biryza gas laser device was found to be safe, with the level of diffusely reflected laser radiation in the work-place much lower than the maximum acceptable levels. The results indicated that labor conditions for personnel working with gas laser devices depend on the effectiveness of hygienic planning in the design and development of models in addition to the observation of safety standards when selecting sites for the gas laser devices. Finally, recommendations are made for avoiding the harmful effects of laser radiation. Tables 2; references 3; Russian.

Maximum Permissible Level of Laser Radiation With a Wavelength of 10.6 Microns

917C01011 Moscow *RADIOBIOLOGIYA* in Russian
Vol 30 No 4, Jul-Aug 90 pp 512-516

[Article by I. N. Ushkova, N. N. Petrishchev, L. A. Pokrovskaya, G. N. Kuzminskaya, L. P. Rodionova, L. P. Usova, V. B. Dul'skiy, L. L. Goncharova, N. Yu. Malkova and A. N. Stankevich, Leningrad Scientific Research Institute of Labor Hygiene and Occupational Diseases, Leningrad Medical Institute No 1, Leningrad Public Health Medical Institute and Leningrad Toxicology Institute]

UDC 577.391.621.375.8

[Text] Local and general reactions of the organism to 10.6 μ laser radiation at an exposure energy level equal to one-seventh of the threshold were studied using 102 male rabbits and 42 HRS/Y mice in the course of a 4-month experiment and then 30 days following the experiment. A conclusion is reached concerning the maximum permissible level of radiation.

In [1,2] we determined the maximum permissible level in an acute experiment and conducted physiological and hygienic studies in a production operation manufacturing 10.6 μ lasers. The maximum permissible levels associated with a chronic experiment involving assessment of the state of target organs—the eyes and the skin—and with study of the dynamics of the general adaptive reactions of the animal body, are refined in this paper.

Materials and Methods

The experiments were conducted on 102 male chinchilla rabbits and 42 hairless HRS/Y mice weighing 20 - 25 gm. Rabbits with healthy eyes were used after being subjected to biomicroscopic research in which the corneal epithelium of live animals was stained with 1 percent sodium fluorescein solution. An LGN-703 CO₂ laser with an output power of 30 W served as the radiation source. The radiation was scattered and attenuated by brass and quartz plates, germanium mirrors and reticular attenuators. Rabbit corneas and mouse haunches were irradiated. Exposure energy (EE) was one-seventh of the threshold— $4.2 \times 10^2 \text{ W} \times \text{cm}^2$, the time of daily exposure was 102 seconds, and the duration of the experiment was 120 days. The diameter of the laser spot on the cornea was 0.8 cm [1]. Ophthalmological observations included studying the cornea of live animals by biomicroscopy, measuring intra-ocular pressure tonometrically (Maklakov's method) and conducting rheo-ophthalmography by Katsnelson's method [3]. The unfavorable action of laser radiation upon the skin was assessed from the condition of dermal microcirculatory flow, which was studied with an MLK-1 luminescent contact microscope ("LOMO") in polarized light at a depth of up to 80 μ from the surface of the transilluminated skin. The total number of vessels within the

microscope's field of vision ($\times 88$) corrected to 1 mm^2 , the shape of the vessels and the relative rate of blood flow (uniform, grainy, intermittent, stasis etc.) were determined. The dynamics of general bodily adaptive reactions in rabbits were studied by physiological, biochemical, histological and electromicrographic methods. In order to evaluate systemic circulation in rabbits, a 068 physiograph was used to record respiration, an electrocardiogram using pattern II points of contact, and arterial pressure in the femoral artery; respiration, heart rate, arterial pressure—systolic, diastolic, pulse and mean dynamic, the duration of the expulsion phase, the stroke and minute blood volumes, and total peripheral resistance were calculated. Autonomic regulation of cardiac activity was analyzed by variational pulsometry. The state of the antioxidant system was used as an indicator of the body's nonspecific resistance. Amperometric titration was used to determine the concentration of thiol and disulfide groups in the protein and nonprotein fractions of blood hemolysate, the thiol-disulfide coefficient was calculated, and the activity of glutathione reductase (GR), glucose-6-phosphate dehydrogenase (G6-PDH), lactate dehydrogenase and blood catalase were determined spectrophotometrically. The analyses were made prior to laser irradiation, on the 5th, 10th, 30th, 60th, 90th and 120th days of exposure, and on the 30th day of the recovery period. After 120 days of the experiment and after 30 days of the recovery period, some divisions of the visual analyzer were studied with an electron microscope: cornea, retina, lateral geniculate body and the visual cortex; the ultrastructure of the lateral hypothalamic field was also studied in its function as the center of autonomic regulation of the cardiovascular system. Histological studies were also conducted on the heart, liver, adrenal glands (hematoxylin and eosin staining) and testes (Heidenhain's hematoxylin staining). The functional state of the adrenal glands was assessed from the relative size of cells in the fascicular zone, for

which purpose the number of cells in the fascicular zone of the adrenal cortex was calculated per standard unit area. The activity of spermatogenesis in the testes was assessed from the number of tubules in different stages of spermatogenesis, using the classification in [4]. Experimental results were compared with similar parameters in animals of the control groups, which were not exposed to laser radiation. All animals were adapted to the experimental conditions. The results of the experiments were treated by probit analysis [5] and Student's t-test with $p < 0.05$.

Result and Discussion

Analysis of the results of eye research showed that areas of desquamation of the corneal epithelium occur in 100 percent of the cases after five irradiation sessions, and that it persists throughout the entire exposure period. Clouding of the cornea was revealed in 17 percent of the cases on the 120th day of the experiment and in 100 percent of the cases on the 30th day of the recovery period. In addition to this, ultrastructural changes were observed in cells of the cornea's endothelial layer. The entire complex of changes, including redistribution of nuclear chromatin, breakup of polysomes into individual ribosomes and partial disorganization of cytoplasmic structures, indicates a decline in synthetic processes and disturbance of nuclear-cytoplasmic relationships. Investigation of other structural elements of the eye did not reveal any kind of pathological changes, including in the retina's nerve components.

Rheo-ophthalmographic data indicate an increase in filling of the eye's uveal tract with blood until the 60th day of the experiment, followed by a decline in the amplitude of the pulse wave by the 120th day of the experiment and on the 30th day after exposure was terminated (Table 1). Investigation of intra-ocular pressure did not reveal significant differences in comparison with both the initial state and data for the control group of animals.

Table 1. Amplitude of the Rheographic Curve (ohms) of the Vascular Tract of the Rabbit Eye During the Experiment ($M \pm m$)

Animal group	Time of Exposure, Days			
	0	30	60	90
Experiment	0.285 ± 0.008	$0.277 \pm 0.008^*$	$0.281 \pm 0.004^*$	$0.246 \pm 0.006^*$
Control	0.250 ± 0.008	0.280 ± 0.008	0.290 ± 0.006	0.214 ± 0.004
Animal group	Time of Exposure, Days			
	60	90	120	Recovery
Experiment	$0.273 \pm 0.007^*$	0.254 ± 0.010	0.229 ± 0.007	$0.164 \pm 0.005^*$
Control	0.217 ± 0.003	0.277 ± 0.006	0.346 ± 0.010	0.246 ± 0.007

*Significant difference compared to the control group.

Table 2. Increase in Vascular Density Depending on Exposure Energy and Irradiation Time (Percent of Cases)

Exposure Energy, W/cm^2	Exposure Time, sec	Analysis Time After Irradiation, hr			
		1	2	3	4
4.2×10^{-2}	10 ²	96	96	96	96
2.1×10^{-2}	10 ²	33	96	96	96
1.0×10^{-2}	10 ²	96	96	96	96

Table 3. Change in Vascular Density in Mouse Skin Depending on Exposure Time (Absolute Value Per 1 mm²)

Animal Group	Exposure Time, days					
	0	5	10	30	60	75
Experiment	50.4 ± 0.30	84.8 ± 0.35*	84.9 ± 0.34*	83.4 ± 0.31*	81.0 ± 0.31*	88.4 ± 0.3*
Control	50.2 ± 0.20	50.3 ± 0.14	50.6 ± 0.13	50.3 ± 0.13	50.1 ± 0.22	48.9 ± 0.32

*Significant differences compared to the control group ($p < 0.05$).

When mouse skin was subjected to the action of reflected radiation with EE equal to one-seventh of the YcD_{50} [not further identified] for the eyes, dermal microcirculation was disturbed in 100 percent of the cases. In this connection, an acute experiment was conducted to determine the threshold of one-time harmful action upon the skin. The EE was varied from 1.0×10^{-2} to $4.2 \times 10^{-2} \text{ W} \times \text{cm}^{-2}$ at a fixed time of action of 102 sec (Table 2).

A YcD_{50} equal to $2.5 \times 10^{-2} \text{ W} \times \text{cm}^{-2}$ (0.017 - 0.037) was determined by probit analysis. The accumulation coefficient is equal to 3.0 at the threshold level.

Disturbances in dermal microcirculation were revealed by a chronic experiment in which mouse skin was exposed to threshold EE (Table 3). Changes in the nature of circulation are noted at all times of analysis on the background of a dependable increase of vessel density in the upper layer of the dermis in animals of the control group: It is slow, grainy and irregular. The vascular channel is cellular in nature, capillary length decreases, ampule-like dilations are noted in vessels, and then convolutedness increases. By the 90th day of action, macroscopically visible damage to upper layers of the skin, followed by deformed scarring, develops in the exposed area in 60 percent of animals, and in 100 percent of animals by the 120th day.

The action of the investigated EE of laser radiation is confirmed by presence of general adaptive reactions by the body. Thus on the 10th and 30th days of the experiment, analysis of data pertaining to systemic circulation revealed a hypertensive reaction of a hyperkinetic type, accompanied by respectively a 54 percent and 62 percent increase in minute blood volume, coupled with a 49 percent and 51 percent decrease in total peripheral resistance; this condition persisted throughout the entire time of the experiment ($p < 0.05$). Cardiointer alometric data revealed dominance of the sympathetic division of the autonomic nervous system in regulation of cardiac activity. The stress index in the experimental group of animals increases throughout the entire experiment, exceeding the same in the control group by a factor of 2.7 in the recovery period ($p < 0.05$).

Dystrophic changes were found to develop in rabbit heart muscle on the 120th day of exposure. The functional activity of the adrenal cortex decreases. This conclusion is based on an increase in the number of cells in the fascicular zone by the 120th day of exposure and by the 30th day of the recovery period.

At the same time, the ultrastructure of the lateral hypothalamic field does not differ from normal.

The function of the antioxidant system is directed at eliminating products of free-radical oxidation and maintaining the oxidation-reduction equilibrium in the living system. A 35 percent increase in the activity of blood catalase by the 5th day of exposure in comparison with control ($p < 0.05$) is evidence of intensification of free-radical oxidation in response to laser irradiation. A 52 - 54 percent rise in the activity of Gl-6-PDH and a 30

31 percent increase in the activity of GR by the 5th - 30th days of the experiment ($p < 0.05$) indicate simultaneous activation of regulatory enzymatic systems. By the 30th day of exposure a 46 and 22 percent statistically significant increase in the concentration of thiol groups and a 68 and 17 percent increase in the concentration of disulfide groups are noted in the thiol-disulfide system of protein and nonprotein blood fractions respectively; the oxidation-reduction equilibrium remains stable in this and subsequent periods. Attainment of equilibrium in the thiol-disulfide system may be explained not only by the action of the enzymes regulating this system—Gl-6-PDH and GR—but also by greater synthesis of reduced thiols, since by the end of the experiment the activity of Gl-6-PDH returns to normal, while the activity of GR decreases to 55 percent by the 60th day ($p < 0.05$), and returns to the control level by the 90th - 120th day. The recovery period is characterized by a new increase in activity of Gl-6-PDH to 132 percent ($p < 0.05$) in comparison with control.

The recovery period is characterized by a new increase in activity of Gl-6-PDH to 132 percent ($p < 0.05$) in comparison with control.

Histological analysis of testes and liver does not reveal significant changes.

There are no differences in the ultrastructure of the lateral geniculate body of control and experimental animals. However, signs of change in individual synapse ultrastructures were discovered in the visual cortex (field 17), which may be evidence of a decrease in the effectiveness of synaptic transmission (osmophilia and polymorphism of the synaptic vesicles of some axon terminals). Moreover, so-called compressed mitochondria are encountered in the neuron cytoplasm. These mitochondria produce three times less ATP than "ordinary" mitochondria, which is responsible for the decrease in the intensity of oxidation-reduction processes in the nerve cell.

Thus an EE equal to $4.2 \text{ J} \times \text{cm}^{-2}$ is effective in the conditions of a chronic experiment, since significant changes were revealed not only during exposure but also

in the recovery period, 30 days after exposure to radiation was terminated, in the eye, the skin, the cardiovascular and antioxidant systems, the visual cortex of both hemispheres (field 17) and the adrenal cortex.

However, changes in the cornea revealed after the recovery period are a reflection of metabolic processes that apparently include disturbance of protein and enzyme synthesis; changes in the skin are associated with microcirculatory disturbances. At the same time, the state of the cardiovascular and antioxidant systems indicates that they participate in adaptive processes. Maintenance of the stability of the oxidation-reduction equilibrium in the thiol-disulfide system is evidence that this system offers a rather strong response to such exposure.

Development of adaptive reactions in response to exposure to this EE is evidence of the organism's capability for preventing transition of metabolic processes into pathological ones, which is what allowed us to establish a safety factor of 2.

Thus according to the experimental data, the maximum permissible level is $1.3 \times 10^{-2} \text{ W} \times \text{cm}^{-2}$ (for a 102 sec exposure time).

Comparison of EE's having an effect in chronic experiments with EE's recorded in work areas shows that they are magnitudes of the same order, and that they elicit disorders of varying degrees of manifestation both in the human body [2] and in the animal body. This confirms the correctness of introducing a safety factor of 2 when substantiating the maximum permissible level.

Consequently the mean monthly maximum permissible level for reflected laser radiation with a wavelength of 10.6μ is equal to $1.3 \times 10^{-2} \text{ W} \times \text{cm}^{-2}$.

According to the "Sanitary Norms and Regulations" [6], the maximum permissible limit is $4.03 \text{ J} \times \text{cm}^{-2}$ (obtained by calculation), and according to the IEC standard "Radiation Safety of Laser Articles, Equipment Classification, Requirements and Guide to Users" [7], it is $0.1 \text{ W} \times \text{cm}^{-2}$.

Bibliography

1. Ushkova, I. N., Dulskiy, V. B., Malkova, N. Yu. and Martenko, E. I. *RADIOBIOLOGIYA*, Vol. 28, No. 6, 1988, pp. 841-842.
 2. Ushkova, I. N., Grishina, Ye. I., Yefimova, M. G. et al. *GIGIYENA I SANITARIYA*, No. 7, 1987, pp. 32-35.
 3. Katsnelson, L. A., "Reografiya glaza" [Rheography of the Eye], Moscow, Meditsina, 1977, p. 119.
 4. Leblond, C. P. and Clermont, J., *AMER. J. OF ANATOMY*, Vol. 90, No. 2, 1952, pp. 167-216.
 5. Prozorovskiy, V. B., *FARMAKOLOGIYA I TOKSIKOLOGIYA*, No. 1, 1962, pp. 115-120.
 6. "Sanitarnyye normy i pravila ustroystva i ekspluatatsii lazeryov No. 2392-81" [Sanitary Norms and Regulations on Laser Design and Operation, No. 2392-81], Moscow, VINITI, 1982, p. 53.
 7. IEC Standard: "Radiation Safety of Laser Articles, Equipment Classification, Requirements and Guide to Users," Geneva, 1987, p. 92.
- COPYRIGHT: Izdatelstvo "Nauka" "Radiobiologiya", 1990.

Management of Severe Brucellosis With Xenobiosorption

917C00234 Moscow *KLINICHESKAYA MEDITSINA* in Russian Vol 68 No 6, Jun 90 (manuscript received 9 Oct 89) pp 110-112

[Article by L. Ye. Tsirelson, T. A. Popov, S. N. Gabidullina, T. A. Grushina, and V. G. Slesarev, Brucellosis Clinical Department, Epidemiology, Microbiology, and Infectious Diseases Scientific Research Institute, Alma-Ata; Clinical and Experimental Surgery Scientific Research Institute imeni A. N. Syzganov; Kazakhstan Clinical Hospital for Second World War Veterans, Alma Ata]

UDC 616.98:579.841.93]-036.17-085.361.41-036.8

[Abstract] Clinical description is presented of a patient with severe brucellosis that did not respond to traditional brucellosis therapy. Following 6 weeks of unsuccessful treatment, xenobiosorption employing a porcine spleen was investigated as a possible means of managing brucellosis. The subclavian vein of the patient was connected to the porcine splenic artery and the porcine splenic vein to the cubital vein of the patient. The session lasted 52 min with 2,340 ml of blood perfused through the porcine spleen. One day after the procedure the patient's temperature had decreased to 37.5°C, and he noted less pain in the joints. By day 2, his temperature had decreased to 37.1°C and pain was lessened even more, lymph nodes could not be palpated, and heart tones were clearer. Five days subsequent to the xenosorption procedure the patient was discharged. Observations for the following 12 months revealed no signs of recurrence. The data demonstrate that this technique merits further attention. References 1: Russian.

Progress in Introducing Sorption Therapy for Radiation Victims

917C01254 Kiev *PRAVDA UKRAINY* in English No 240, 18 Oct 90 p 4

[Interview with V.G. Nikolayev, professor of Institute of Problems of Oncology imeni Kavetskiy, a USSR State Prize laureate and member of New York Academy of Sciences]

[Abstract] The article is an interview with Vladimir Grigoryevich Nikolayev, a professor of the Ukrainian Academy of Sciences' Institute of Problems of Oncology imeni Kavetskiy, a USSR State Prize laureate and a member of the New York Academy of Sciences. Nikolayev traces the history of work which he and his colleagues have been doing on development and introduction of sorption methods for treatment of persons exposed to radiation.

When his group began its work in this direction, much research of the effects of radiation on living organisms was still secret, Nikolayev recalls. A hemosorption

method for treatment of absolutely fatal cases of radiation injury was tested on animals in 1976. Radiotoxins which form as a result of interaction between radiation and living structures were removed from the blood extracorporeally, using a sorbent in a column. Experiments were conducted with the participation of Doctor of Medical Sciences L. B. Pinchuk, who was then on the staff of the Ukrainian Ministry of Health's Kiev Scientific Research Institute of Hematology and Blood Transfusion. These experiments yielded unprecedented results. Up to 80 percent of the animals which received sorption therapy during the first 24 hours following irradiation survived. During the late 1970s, this direction of research was advanced at the USSR Academy of Sciences' Institute of Biophysics and at clinical and research centers in Leningrad, Kiev, Gorkiy, Chelyabinsk and other cities. In 1982, at a closed conference at the biophysics institute, Nikolayev reported on results of treatment of acute radiation injuries by an enterosorption method. This approach received advancement at the Military Medical Academy. Early in the 1980s, a clinical base facility of Nikolayev's laboratory in Kiev became a republic hospital of the State Security Committee (KGB). New methods of sorption therapy were tested and utilized here. A considerable amount of experience with the new methods had thus been amassed by April 1986, when the accident occurred at the Chernobyl Nuclear Power Station.

Nikolayev relates that shortly after this accident, he telephoned academician Leonid Andreyevich Ilin, director of the biophysics institute, offering to set up several hemosorption stations in Kiev, but the offer was rejected. Ilin and his colleagues considered a method of bone-marrow transplantation more effective than sorption for treatment of radiation victims. Nikolayev explains. At that time, no direct information was available on results of the Kiev scientists' therapy in cases of chronic irradiation, including irradiation from radionuclides in the organism. On April 29-30, a group of more than 130 associates of the Chernobyl station and firemen was sent to a clinic of the oncology institute for treatment. Professor I.V. Kasyanenko heads this clinic. All of these accident victims underwent intensive treatment with enterosorbents for a week; some of the patients subsequently received hemosorption therapy. All but one survived. Nikolayev then proposed that sorption methods be utilized as broadly as possible in overcoming medical consequences of the Chernobyl disaster, and the KGB's medical service put them into practice on an extensive scale, with good results. Sorption therapy reportedly has proved effective in speeding removal of radionuclides from the organism and preventing general deterioration of patients' health.

Nikolayev claims that the Soviet Union is maintaining leading positions in sorption therapy. He reports that several versions of medical sorbents have been tested in clinics, and new types of sorbents are under development. Soviet industry's potential for producing sorbents is practically unlimited, according to Nikolayev. The

Pridneprovskiy Chemical Plant, the Brovary Powder Metallurgy Plant, and the "Synthetic Fiber" production association in Svetlogorsk (Belorussia) are mentioned as enterprises which possess suitable capacities for their production. Nikolayev advocates the creation, in Kiev and other cities, of medical-social rehabilitation centers where large numbers of patients could be treated by sorption methods.

Soviet-Vietnamese Joint Enterprises for Homosorbent Production

917C0125B Moscow PRAVDA in English No 294.
21 Oct 90 p 2

[Article by I. Tikhomirov, PRAVDA correspondent, Kiev]

[Excerpt] The scale of an operation called "Coconut" which PRAVDA began is becoming broader day by day. Scientists of the department of sorption and fine inorganic synthesis of the Ukrainian Academy of Sciences' Institute of General and Inorganic Chemistry got the idea of developing and using so-called highly select sorbents for the purpose of removing, from the human organism, radionuclides, heavy metals, pesticides and radiotoxins which are particularly dangerous to health. As often happens, this idea received no support. It took almost four years to rehabilitate a therapeutic preparation.

The attitude toward it has changed noticeably in recent months. The formerly scattered energies of groups involved in producing and introducing this preparation have in turn been concentrated through the creation of a consortium, "Ekosorb." However, only about 2 tons of the preparation can be produced from raw materials which are now available, and tens of times as much is required.

Vietnamese scientists and specialists put forward the idea of creating at least two joint Soviet-Vietnamese enterprises in regions of palm plantations and producing the preparation there.

This idea was put into practice right away. Talks between S. Burlachenko, vice-president of the joint-stock company "Unknown Cosmodrome"; N. Ilyasov, general director of the Ukrainian "Asso-Unity" association, who represents the interests of the "Ekosorb" consortium; and representatives of the Vietnamese embassy in the USSR took place recently in Kiev. The question was discussed of creating joint enterprises for producing medicinal preparations and other products from coconut shells. In the process of negotiations, the two sides reached agreement on all questions of mutual interest and set specific deadlines for resolving them. A group of Soviet specialists will leave for Vietnam during the next few days, for the purpose of creating joint enterprises. Production of preparations which are sorely needed for persons stricken at the time of the accident at the Chernobyl Nuclear Power Station will be organized in the course of a year.

Antibiotic Therapy of Armenian Earthquake Victims With Crush Injuries

917C0140B Moscow ANTIBIOTIKI I
KHIMIOTERAPIYA in Russian Vol 35 No 10, Oct 90
(manuscript received 12 Mar 90) pp 21-24

[Article by E. A. Nechayev, I. D. Kosachev, V. I. Kocherovets and M. V. Yepifanov, Military Medical Academy imeni S. M. Kirov, Leningrad]

UDC 615.33.03:617-001.4-002.3-022.7-
02:550.348.436+617-001.4-002.3-002.7-
02:550.348.436]-085.33][479.25]

[Abstract] An analysis was conducted on antibiotic management of 88 victims of the Armenian earthquake with crush injuries. The patients were treated for pyogenic wound infections. Sensitivity testing demonstrated that appropriate antibiotics were employed in only 18.2 percent of the cases, while ineffective antibiotics were used in 55.7 percent. In general, 80 - 100 percent of the isolates were resistant to antibiotics usually employed in surgical practice, consisting of penicillins, aminoglycosides and their combinations. Lack of familiarity with the more efficacious ureidopenicillins and quinoline drugs was the key factor precluding their use. Tables 3; references 7: 6 Russian, 1 Western.

Device for Personal Prevention of Sexually Transmitted Diseases

917C0128B Minsk ZDRAVOOKHRANENIYE
BELORUSSII in Russian No 10, Oct 90 (manuscript
received 15 Feb 90) pp 60-61

[V. G. Pankratov and R. N. Pilkevich, Chair of Dermatology and Venereology, Minsk Medical Institute, Minsk Municipal Clinical Dermato-Venereologic Public Health Clinic]

UDC 616.97:616-084

[Abstract] A new and improved device for personal prevention of sexually transmitted diseases following casual sexual contact has been designed based on the previously manufactured pocket device for preventing venereal diseases. This device is accessible and easy to use. Instructions for using the device include removing the safety cap, putting on the nozzle, filling the bulb with disinfectant (preferably chlorhexidine bigluconate (hibitane) or miramistin [sic]), and applying the disinfectant to the genitals. It is best if used within 30 minutes of contact; however, it may be effective up to 2 hours later. The device is recommended for widespread use, including among the army and naval and commercial fleets. Figures 1; references 3; Russian.

Surgical Strategy in Landmine Trauma

917C0134A Leningrad VESTNIK KHIRURGII IMENI
I. I. GREKOVA in Russian Vol 145 No 10, Oct 90
(manuscript received 31 Jan 90) pp 51-55

[Article by L. N. Bisenkov and Ye. K. Gumanenko, Military Medical Academy imeni S. M. Kirov, Leningrad]

UDC 622.2/.3:616-001-089-035

[Abstract] A generalized approach to surgical management of trauma caused by landmine explosion is considered, with emphasis on the fact that surgical intervention has to be based on an understanding of the systemic nature of the injuries. The importance of a clear understanding of the pathophysiologic mechanisms underlying the wounds and injuries cannot be overestimated if rational preoperative management and triage are to be practiced and appropriate surgery to be subsequently undertaken. Surgeons are cautioned against simultaneous multiple operations except in cases based on the highest order of expert opinion, because of additional stress placed on an already exhausted organism depleted of its vital reserves. Experience has shown that successive operations within one anesthesiologic interlude appear to be much better tolerated.

Hemosorption-Facilitated Healing of Severe Burns

917C0134B Leningrad VESTNIK KHIRURGII IMENI
I. I. GREKOVA in Russian Vol 145 No 10, Oct 90
(manuscript received 27 Feb 89) pp 57-60

[Article by N. Ye. Povstyanov and A. F. Fedotov, professors, G. P. Kozinets and V. I. Neulybin, Kiev Institute of Advanced Training for Physicians; Kiev Scientific Research Institute of Hematology and Blood Transfusion]

UDC 616-001.17-085:615.38.66.081

[Abstract] Histological assessment of wound healing in relation to hemosorption was studied in the case of 19 patients, 20 - 60 years old, with 3rd to 4th degree burns over 25 - 65 percent of the body surface. Thirteen control burn patients were managed in a conventional manner without hemosorption. Hemosorption was employed 4 - 10 days after trauma in the veno-venous mode to encompass one third of the circulating blood volume at a flow rate of 64 ml/min. The histologic studies and clinical outcome demonstrated that 1 - 4 hemoperfusions facilitated wound healing and earlier recovery, with epithelialization occurring in 16 - 21 days (3 - 4 days earlier than in the control patients with analogous injuries). In addition, the area of epithelialization was 15 - 20 percent greater than in the control patients, providing further impetus for the use of intensive detoxication in burn cases. Figures 4; references 1; Russian.

Determination of Microbial Sensitivity to Antiseptics

917C0134C Leningrad VESTNIK KHIRURGII IMENI
I. I. GREKOVA in Russian Vol 145 No 10, Oct 90
(manuscript received 13 Oct 89) pp 106-107

[Article by V. M. Buyanov, G. V. Rodoman, A. A. Khrupalov, Ye. V. Stetsenko and A. L. Korotayev, Chair of General Surgery, Therapeutics Faculty, 2nd Moscow Medical Institute imeni N. I. Pavlov]

UDC 616-001.4-008.87:615.28].002.1

[Abstract] A technique was devised for testing bacteria for susceptibility of common antiseptics, based on a modification of the tube dilution test for assessing antibiotic resistance. In its essential features, the method involved preparation of test tube suspensions of the bacteria and monitoring their growth in Hottinger's medium by OD measurements. Addition of bacteriostatic antiseptics precluded an increase in OD, while antiseptics with lytic activity actually led to a decrease in OD. Studies with isolates obtained from the wounds of 145 patients showed that apolam, formulation C-4, aseptol, and chlorhexidine were the most effective antiseptics against golden staphylococcus, E. coli, Ps. aeruginosa and mixed flora. Furacilin was found to be completely ineffective. Tables 1; references 2; Russian.

Protective Activity of Mexamine in Rats Following Electromagnetic Irradiation

917C00971 Moscow KOSMICHESKAYA BIOLOGIYA I L AVIAKOSMICHESKAYA MEDITSINA in Russian
Vol 24 No 4, Jul-Aug 90 (manuscript received 24 Jul 89)
pp 55-56

[Article by S. A. Bugrov, B. I. Davydov, V. S. Tikhonchuk, S. K. Soldatov, and T. F. Osokina]

UDC 616-001.28-036.88-02:615.849.112]-
092.9+615.849.112.015.25.03:616-001.28-
036.88-02:615.849.112]-084

[Abstract] Previous studies have demonstrated the protective effect of mexamine on ionizing radiation exposure and in enhancing resistance to hypoxia. In this investigation, the protective effects of mexamine following powerful ultrahigh frequency (UHF) electromagnetic irradiation were researched on 230 female rats (250 - 300 g). The subjects were administered mexamine hydrochloride in doses of 1, 5, and 15 mg/kg, intraperitoneally. They were then irradiated 5 min, 20 min, 1 h,

or 2 h later in an echo-proof chamber with 2.4 GHz of electromagnetic radiation for 3 min. Calculations indicated that the specific absorption capacity of the rats ranged from 450 mW/cm² to 525 mW/cm². During microwave irradiation, the rats were restless and agitated and progressed into localized or generalized convulsions by the end of the radiation period. The results demonstrated that animals irradiated 20 min and 1 h after mexamine administration had survival rates of 71 and 88 percent, respectively, as opposed to a 35 percent survival rate for control animals. Rats irradiated 2 h subsequent to mexamine administration did not exhibit any signs of the protective effect of mexamine, while rats irradiated 5 min after mexamine administration actually had a survival rate of only 6 percent. The protective effect of mexamine administered 20 min and 1 h prior to irradiation was attributed to hypothermia, which is one of the reasons for the preparation's protective effect. The pathobiochemical protective mechanism of mexamine on UHF irradiation remains unclear and awaits further research. Figures 1, tables 1; references 10; 5 Russian, 5 Western

Antiretroviral Drug Developed at Armenian Institute

917C0067 Moscow MOSCOW DOMESTIC SERVICE
in Russian 12 51 GMT 29 Jul 90 pp 1-2

[Editorial Report]

[Text] Yerevan correspondent Koryun Khumaryan reports (voice) on an anti-AIDS compound developed in Armenia. Interviewed at the Research Institute of Experimental Biology of the Armenian Academy of Sciences in Yerevan, Konstantin Grigoryevich Karagezyan, the institute director, says that the compound has a "nonspecific, but anti-viral action" and "considerably enhances" the activity of interferon. Robert Aramaisevich Zakharyan, a laboratory chief at the institute, says: "We conducted experiments in our conditions here, which confirmed that the compound is effective against viruses which are similar in origin to the AIDS virus—the so-called retroviruses." He says that it was sent to Professor Arag Avanesyan at the Pasteur Institute for testing. "According to data received, the compound has proved encouraging for clinical use." Professor Akopyan, chief of the institute's molecular enzymology laboratory, says that "the compound actually slows down the reproduction of the virus in cells by 83 percent" compared to a figure of 25 - 37 percent for AZT, and whereas a course of treatment with AZT costs \$400 - \$450 per patient, "a dose of our compound according to economic assessments, preliminary ones of course, costs 13 - 20 kopecks."

Effect of a Perfluorocarbon Emulsion—An Inducer of Enzymes of the Liver's Cytochrome P-450-Dependent Monooxygenase System—on Acute Toxicity of CCl_4 and on the Effectiveness of Preventive Use of Antidotes in Organophosphorus Pesticide Intoxications

917C0094A Moscow FARMAKOLOGII I
TOKSIKOLOGII in Russian Vol 53 No 4, Jul-Aug 90
pp 60-62

[Article by G. M. Mikhaylov, A. A. Varykhanov, L. A. Omarova, V. Ye. Verovskiy and V. V. Obratsov, Institute of Biological Physics of the USSR Academy of Sciences, Pushchino, Moscow Oblast, 142292, Institutskaya]

UDC 615.285.7.099.036.11.085.355

[Text] Research was conducted on the effect of intraperitoneal administration of perfluorocarbon emulsion—an inducer of the liver's cytochrome P-450-dependent monooxygenase system—on the resistance of rodents to the effect of CCl_4 and organophosphorus pesticides. The perfluorocarbon emulsion potentiated the toxicity of CCl_4 , decreasing the LD_{50} from 4.5 to 3.7 ml CCl_4 per kilogram of mouse body weight; however, it was unable to change susceptibility of rats to organophosphorus pesticides on its own. Preliminary administration of perfluorocarbon emulsion effectively raised the protective action of antidotes (atropine + diptyroxime), making the animals resistant to 12-fold, 20-fold and 20-fold LD_{50} concentrations of dichlophos, methaphos and butiphos respectively.

Introduction

The idea of pharmacologically utilizing induction of enzymes of the liver's cytochrome P-450-dependent monooxygenase system was proposed by A. Conney over 20 years ago [9]. The activity and quantity of the enzymes of the monooxygenase system of liver microsomes, which take part in oxidative metabolism of a number of foreign and endogenous compounds, are known to be significantly higher when hydrophobic xenobiotic compounds are introduced into the organism. But even today there still is interest in capitalizing on the phenomena associated with induction of microsomal monooxygenase with the purpose of treating and preventing a number of diseases and intoxications. But the principal obstacle to realizing Conney's ideas has been that all hydrocarbon xenobiotics—be they inducers or their hydroxylation products—possess physiological activity as a rule: that is, besides inducing cytochrome P-450, they evoke narcotic sleep, exert specific therapeutic action, or act as poisons, particularly as carcinogens. In this sense completely fluorinated organic compounds—perfluorocarbons, the capacity of which for elevating the activity of the monooxygenase system by way of induction of cytochrome P-450 was recently demonstrated [2,5-8,12]—are the most neutral compounds satisfying the requirements of a "non-drug" xenobiotic-inducer. In view of high chemical inertia, these compounds are not metabolized, and their introduction into the animal body in large quantities produces minimum side effects [1,7,11]. Synthesis of the "phenobarbital" form of cytochrome P-450 in the animal's liver in response to introduction of perfluorocarbons into its body [2] may significantly alter the traditional pharmacokinetics and pharmacodynamics of compounds that undergo oxidative metabolism with the participation of microsomal monooxygenase. An attempt was made on the basis of this proposal to study the influence of perfluorocarbon inducers on the acute toxicity of CCl_4 and organophosphorus pesticides.

Research Methods

The experiments were conducted on white mongrel mice and rats. A 10 percent submicron emulsion of perfluororganic compounds by volume, containing perfluorodecalin and perfluoro-p-methyl-cyclohexylpiperidine in a 2:1 ratio, was used as the agent inducing cytochrome P-450 in the liver. The emulsion was stabilized with a 4 percent solution of propanol 268. The concentration of ions and glucose in the emulsion corresponded to the concentration of these compounds in blood plasma.

To study acute toxicity of pesticides, the perfluorocarbon emulsion was administered to rats intraperitoneally at a dose of 8 ml/kg, daily for 3 days. Twenty-four hours after the final administration of the emulsion, atropine (10 mg/kg) and diptyroxime (10 mg/kg) were injected intramuscularly into the animals 20 minutes prior to introducing the pesticides.

To study acute toxicity of CCl_4 , it was administered to mice intragastrically by means of a probe. The perfluorocarbon emulsion was simultaneously administered intraperitoneally at a dose of 10 - 20 ml/kg. An equivalent quantity of

solution containing all emulsion components except perfluorocarbons was used in the control. All solutions were prepared in aseptic conditions. Animals that lived 7 - 14 days were assumed to have survived.

Results and Discussion

The table gives data on the effect of preliminary administration of perfluorocarbon emulsion on the effectiveness of antidote prevention in rats poisoned with dichlophos, methaphos and butiphos. As is evident from the table, the perfluorocarbon emulsion itself is not an antidote—that is,

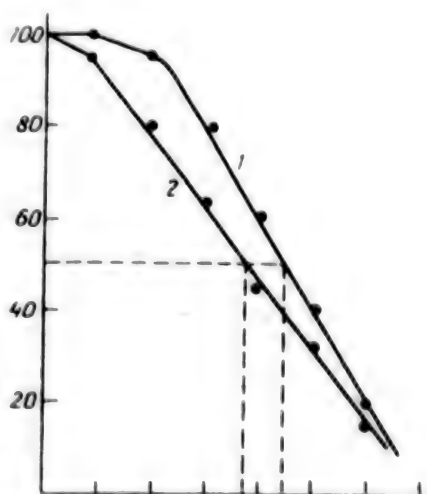
administration of perfluorocarbons does not avert the death of animals. Use of the antidotes, atropine and dipyroxime, is effective in the prevention of not more than six LD₅₀ of organophosphorus pesticides. However, the significant increase in protective action of antidotes on the background of preliminary administration of perfluorocarbon emulsion is a fact that attracts the greatest attention. Thus, administration of the emulsion and the combination of antidotes to animals makes rats resistant to 12-fold, 20-fold and 20-fold DL₅₀ concentrations of dichlophos, methaphos and butiphos respectively.

Effect of Perfluorocarbon Emulsion on Acute Toxicity of Organophosphorus Pesticides

Pesticide	Dose, Multiple of DL ₅₀	Preparations Administered Preliminarily	Time of Mass Die-Off, min	Proportion of Surviving Animals, %	Number of Animals
Dichlophos	3	Perfluorocarbon emulsion	3	0	6
	6	Atropine + dipyroxime	-	100	6
	9	Atropine + dipyroxime	15	0	6
	12	Perfluorocarbon emulsion + atropine + dipyroxime	-	100	15
Methaphos	3	Perfluorocarbon emulsion	3	0	6
	6	Atropine + dipyroxime	-	100	6
	12	Atropine + dipyroxime	7	0	6
	20	Perfluorocarbon emulsion + atropine + dipyroxime	-	100	10
	34	Perfluorocarbon emulsion + atropine + dipyroxime	20	33	15
Butiphos	3	Perfluorocarbon emulsion	3	0	6
	12	Atropine + dipyroxime	15	0	6
	20	Perfluorocarbon emulsion + atropine + dipyroxime	-	100	6
	34	Perfluorocarbon emulsion + atropine + dipyroxime	10	33	15

The opposite pattern was revealed when perfluorocarbon emulsion was administered to animals poisoned with CCl₄. It is readily evident from the figure that the emulsion potentiates the action of CCl₄, reducing the LD₅₀ from 4.5 to 3.7 ml CCl₄ per kilogram of mouse body weight. It should be noted that the negative effect in the action of perfluorocarbon emulsion is expressed to a greater degree at low CCl₄ doses, and it is practically neutralized at high doses.

These data are clear evidence that perfluorocarbons are capable of altering the resistance of animals to toxic effects. It is well known that different xenobiotics form both less toxic and more toxic products relative to the initial compounds in the course of biotransformation involving participation of the cytochrome P-450-dependent monooxygenase system [3]. From this point of view, potentiation of the toxic reaction of CCl₄ by perfluorocarbon emulsion is fully understandable, inasmuch as CCl₃ radicals, formed in monooxygenase reactions with the participation of cytochrome P-450, is the principal destructive agent in CCl₄ intoxications [4]. The iso-form of cytochrome P-450, which appears in the animal organism in response to administration of phenobarbital, displays high activity in relation to this oxidative modification of CCl₄ [13]. Thus the toxic action of CCl₄ is potentiated by perfluorodecalin—an



Survival of Mice After Administration of CCl₄:
abscissa—CCl₄ dose (ml/kg), ordinate—percent of animals surviving. 1—control; 2—administration of perfluorocarbon emulsion. Dots on the curves correspond to the average of a group of 10 - 20 animals

inducer of the "phenobarbital" iso-form of cytochrome P-450 [2], contained in the emulsion

A different pattern of action of perfluorocarbon emulsion is observed when animals are poisoned by organophosphorus pesticides. Despite the fact that perfluorocarbon emulsion does not itself possess antidote properties with respect to pesticide intoxication, its use together with traditional antidotes, is extremely effective. Absence of direct protective action of perfluorocarbons and highly effective action when used jointly with certain preparations, where one is a cholinolytic and the other is an acetylcholinesterase reactivator, is evidence of a complex molecular mechanism behind the observed phenomenon. It may be hypothesized that induced enzymes of the liver's monooxygenase system are capable of changing the pharmacodynamics of antidotes and modifying the processes of metabolism and detoxification of organophosphorus pesticides. Moreover, besides causing specific changes associated with synthesis of the iso-form of cytochrome P-450, inducers are also known to noticeably influence other aspects of cell metabolism [10]. In particular, when perfluorocarbon emulsions are administered to animals, a relative increase in liver weight is observed, resulting from hypertrophy and hyperplasia of hepatocytes [15], cholinesterase activity rises, and the activity of succinate and lactate dehydrogenase, NADP-diaphorase and other liver enzymes decreases [1,14,15].

Thus we were able to show that administration of an emulsion of completely fluorinated organic compounds significantly increases the effectiveness of antidotes in relation to intoxication by organophosphorus pesticides in supertoxic doses. The discovered effect is apparently the product of not only the unique capacity of perfluorocarbons for inducing "phenobarbital" iso-forms of cytochrome P-450, but also by their capacity to activate, by means of induction, certain adaptive programs for the expression of genes for the set of enzymes involved in phase II detoxification, particularly glutathione-S-transferase, uridine diphosphate glucuronyl transferase and others.

Oxygen-transporting blood substitutes based on perfluorocarbon emulsions are used successfully in various clinical situations, and in addition to modified hemoglobin, perfluorocarbons are now the most useful preparations from which to make general-purpose gas-transporting transfusion media [11]. The opposite action of perfluorocarbon emulsions on the toxicity of various poisons, discovered in this study, should be considered when using perfluorocarbon blood substitutes on the background of various intoxications and pathological states of the liver.

Conclusions

1. Intraperitoneal administration of perfluorocarbon emulsion to mice increases acute toxicity of CCl_4

2. Preliminary administration of perfluorocarbon emulsion to rats enhances the preventive effect of the combination of atropine and dipyroxime against acute intoxication by organophosphorus pesticides

Bibliography

1. Vasilyev, A. E. and Golubev, A. M., "Etoruglerodnyye gasoprenosyashchiye sredy" [Perfluorocarbon Gas-Transporting Media], Pushchino, 1984, pp 130-134
2. Grishanova, A. Yu., Obratsov, V. V., Shekhtman, D. G. and Ivakhovich, B. B. BIOKHIMIYA, Vol 52, 1987, pp 1138-1143
3. Ivakhovich, V. V. and Tsvilov, I. B., "Induktsiya fermentov metabolizma ksenobiotikov" [Induction of Enzymes Involved in Metabolism of Xenobiotics], Novosibirsk, 1982, p 340
4. Golikov, S. N. (Editor), "Neotlozhnaya pomoshch pri ostrykh otravleniyakh. Spravochnik po toksikologii" [First Aid for Acute Intoxications. Toxicology Handbook], Moscow, 1977, pp 210-214
5. Obratsov, V. V., Shekhtman, D. G., Sologub, G. R. and Belovartsev, E. I. BIOKHIMIYA, Vol 50, 1985, pp 1120-1127
6. Obratsov, V. V., Shekhtman, D. G., Sklifas, A. N. and Makarov, K. N., BIOKHIMIYA, Vol 53, 1988, pp 613-619
7. Khlopushina, G. G., Kovalev, I. Ye. and Lysenkova Ye. M., BIOKHIMIYA, Vol 51, 1986, pp 664-667
8. Armstrong, F. H. and Lowe, K. C., J. PHARM. PHARMACOL., Vol 40, 1988, Suppl., pp 1-141
9. Conney, A. H., PHARMACOL. REV., Vol 19, 1967, pp 317-366
10. De Pierre, J. W., Siedegard, J., Morgenstern, R. et al., BIOCHEM. SOC. TRANS., Vol 12, 1984, pp 58-60
11. Geyer, R. P. and Nose, V. et al. (Editors), "Progress in Artificial Organs," Cleveland, 1987, pp 1157-1166
12. Huang, R., Cooper, D. Y. and Sloviter, H. A., BIOCHEM. PHARMACOL., Vol 36, No 24, 1987, pp 4331-4335
13. Lieber, C. S., ENZYME, Vol 37, 1987, pp 45-56
14. Lowe, K. C. and McNaughton, D. C., EXPERIENTIA (Basel), Vol 42, 1986, pp 1228-1231
15. Lutz, J., Metznerauer, P., Kunz, E. et al., and Frev, R. et al. (Editors), "Oxygen Carrying Colloidal Blood Substitutes," Munchen, 1981, pp 73-81

COPYRIGHT: Izdatelstvo "Meditsina", 1990

Psychomotor Stimulants as Performance-Enhancing Drugs

917C0094B Moscow *FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian* Vol.53 No.4 Jul-Aug 90 pp.72-77

[Article by A. V. Smirnov, pharmacology department (acting chairman, Doctor of Medical Sciences A. V. Smirnov), Military Medical Academy imeni S. M. Kirov, Leningrad, 194175, ul. Lebedeva, 6]

UDC 615.214.31.015.4:612.766.1].07

[Text] The purpose of this survey was to examine the mechanisms of action and the main and side effects of pharmacological preparations in the psychomotor stimulant class when used to enhance and maintain performance in various conditions. The patterns of action of these preparations are examined in relation to basic types of work, with regard for the dependence of the effects on the intensity and duration of the loads and presence of complicating factors (emotional stress, hypoxia, high ambient temperature, drastic tiring and overtiring). The general principles of using these drugs in accordance with the appropriate indications are also presented

Although psychomotor stimulants have already been around more than just a single decade, and a number of these preparations are used as the principal means of enhancing performance, there has been little research in which the effects of these preparations on particular forms of activity have been analyzed. Not a single generalizing survey specially devoted to psychomotor stimulants examining in detail all of the issues listed above has been published. The survey below attempts to correct this omission.

Phenylethylamine derivatives have the most pronounced positive effect on performance among psychomotor stimulants. The first effective drugs created on the basis of phenylethylamine were phenamine (amphetamine, benzedrine) and pervitin (methamphetamine). Other stimulants were developed later—pipradrol (metatran), centedrin (methylphenidate), pemoline (azoksonon), thozaline etc. All of these drugs contain phenylethylamine in their molecular structure, in this case, the amine group may be unsubstituted (phenamine) or substituted (pervitin), and it may even disappear when the corresponding nitrogen atom is included in ring systems (pipradrol, centedrin, pemoline, thozaline etc.). Nonetheless, all of these drugs have a basically similar mechanism of action, which permits us to bring them together into the phenylethylamine derivative group, as one of the leading specialists on psychostimulants, J. M. Van Rossum, believes [41]. This group also includes the Soviet drugs, 'sidnokarb' and 'sidnofen', in the molecules of which the phenylethylamine nitrogen atom is included in the sydnominine ring. These drugs can also include a new drug of plant origin katinon (α -aminopropiophenone) [29].

The positive effect of phenylethylamine derivatives on mental and physical performance and on sensomotor operator activity was discovered with phenamine and pervitin back in the 1930s - 1940s [7,11,19,25]. The effectiveness of phenamine and its analogues was confirmed in later research [4,14,15,28,35,36,42,43]. Generalizing the results, we can conclude that the effect of psychomotor stimulants that are phenylethylamine derivatives manifests itself most clearly when we evaluate an indicator of activity such as endurance, that is, the ability to maintain a certain work output over time. This pertains, in particular, to the effects of drugs in the presence of dynamic and, to a lesser degree, static physical loads. For example in the presence of a high dynamic load (running on a treadmill), pervitin at a dose of 15 mg almost doubles the maximum time subjects are able to work [25]. At the most intensive (submaximum and maximum) loads on a bicycle ergometer, the positive effect of pervitin is less pronounced, but it remains extremely significant (from +29 to +61 percent) [43].

Psychomotor stimulants based on derivatives of phenylethylamine are also capable of noticeably lengthening the time of mental and operator activity, and preventing reduction of work quality; moreover, they raise output in these forms of activity and their rate [4,42]. However, at the most intensive loads, the effect of the drugs generally appears to be significantly less positive, inasmuch as the qualitative indicators of work usually not only fail to improve but on the contrary they worsen, and sometimes quite drastically at that [4]. The more intensive and consequently, the more complex performance of mental and operator activity is, the more work quality can suffer. Therefore in the presence of intensive loads, only rather simple forms of mental and operator activity, and activities that have been made automatic, do not worsen in response to these substances; work quality may even improve [13]. It should be emphasized that these drugs also fail to improve qualitative indicators of complex forms of mental and operator activity in cases where the work is not intensive, and it is not carried out under the pressure of time [9,33].

If the action of psychomotor stimulants based on phenylethylamine derivatives is evaluated in the presence of dynamic physical loads on the basis of the rate at which work is carried out (for example on the basis of the time it takes to cover a certain distance), then the positive effect of the drugs reveals itself rather distinctly [35], even though at first glance it may not be very impressive at the most intensive loads. However, we cannot forget that acceleration of maximally stressed physical activity, even for a few seconds and sometimes fractions of a second, corresponds to an extremely significant increment in work output, especially by well-trained persons. Attaining such an increment without drugs requires months and years of persistent training. These stimulants raise work output in the case of power loads as well [42].

Psychomotor stimulants of this group act upon performance quickly—30 minutes to 1 hour after a single dose

[40]. This is why these drugs remain, for the moment, the most effective means of rapidly enhancing performance, barring many of the complications (see below).

The effect of these substances on performance is accompanied by pronounced stimulatory action upon mental state: A sensation of elevated mental and physical activity arises, the person's mood and the way he feels improve, he becomes less drowsy, his self-confidence grows, his volition strengthens, and he comes to feel that his work is easier and more effective [4,37]. Night-time performance is enhanced owing to decreased drowsiness [42].

The effect on performance depends on the degree of tiring which serves as the background for use of the drugs. Their positive action on physical performance is most noticeable in the absence of a fatigue background [13,36]. In the case of mental and operator activity the reverse is true: These drugs enhance performance usually on the background of fatigue [42]. Of course, in such cases, the drugs usually do not evoke a real increase in performance in comparison with the initial level (prior to development of fatigue), or they simply prevent its further decline. These effects are noted if fatigue is not very severe, and at extreme fatigue it is difficult to anticipate positive action from phenamine and its analogues.

The mechanism of action of psychomotor stimulants based on phenylethylamine derivatives is associated with stimulation of adrenergic structures of the central and peripheral nervous system and dopaminergic structures of the central nervous system owing to more intensive release of mediators (norepinephrine and dopamine) from presynaptic endings into the synaptic cleft (indirect dopamino- and adrenomimetic effect), blocking their reverse transport back to the endings, and (to a lesser degree) inhibition of monoamine oxidase, which breaks down mediators [32,41]. The drugs act primarily on subcortical structures—the ascending activating system of the brain stem's reticular formation, the neostriatum, and owing to the stimulatory effect upon these structures, the cerebral cortex is activated secondarily, indirectly [24]. Thus enhancement of mental performance by means of phenylethylamine derivatives is a consequence of not their direct but their indirect action upon the cortex, directed chiefly at attaining a higher basal level of neuron activity. Direct contact of these drugs with cortical cells under experimental conditions even elicits a certain inhibitory effect [38].

The psychostimulatory action of phenylethylamine derivatives manifests itself as elimination or weakening of the sensation of tiredness and intensification of the desire to continue working [4,40]. The effect on motivations is extremely pronounced, such that in early studies enhanced performance was often ascribed exclusively to this effect [19].

All of the indicated aspects of the central action of these drugs doubtlessly have significance in enhancing mental

and physical performance. In the latter case, activation of the motor centers of the central nervous system resulting from primary stimulation of the neostriatum, which then spreads through intermediate links to motor centers of the ventral thalamus and cortex, is very important as well [24].

Intensification of processes associated with mobilizing, delivering and utilizing substances acting as energy sources plays a large role in the effect of phenylethylamine derivatives on performance. Activation of adrenoreceptors by these drugs intensifies glycogenolysis and lipolysis in cells, leading to formation of glucose, glucose-6-phosphate and nonesterified fatty acids used as energy sources [16,26]. Organs that actively function during work utilize both their own intracellular energy stores, and reserves redistributed from other organs, particularly from the liver in the form of glucose and from fat tissue in the form of nonesterified fatty acids. The brain, of course, is known to make almost no use of these acids. Elevated activity of mitochondrial oxidative enzymes promotes greater utilization of mobilized substrates in energy production processes [16].

It is important to emphasize that use of energy resources in response to psychomotor stimulants, based on phenylethylamine derivatives, is uneconomical and exhaustive [13,16,22], inasmuch as intensively produced useful energy (in the form of ATP molecules) is expended in support of not only the work being done but also various energy-dependent processes not having a direct relationship to the given work, and activated by adrenergic stimulation of organs and tissues. For example, the activity of Na^+ , K^+ -dependent ATP-ases in cell membranes, which consume a great deal of energy, rises in many organs under the influence of norepinephrine [27]. Part of this indirectly utilized energy transforms into heat. Moreover, adrenergic mediators (norepinephrine) may have a disengaging effect on mitochondria, directly or indirectly (by releasing nonesterified fatty acids) [12,27], reducing the effectiveness of the cell's principal energy-producing system as a result. These features of the mechanism of action of these drugs explain the considerable loss of energy in the form of heat, which often leads to an increase in body temperature even at rest [10,23].

The increase in physical performance, elicited by psychomotor stimulants based on phenylethylamine derivatives in times of reduced effectiveness of oxidative phosphorylation, is partially supported from an energy standpoint by activation of anaerobic glycolysis—an uneconomical pathway of ATP formation, which is responsible for progressive depletion of energy reserves and accumulation of lactic acid in organs and blood, and aggravation of the effects of acidosis accompanying physical loads [13,43]. Reduction of the efficiency of the system of oxidative phosphorylation in response to an increase in energy demand and elevation of the activity of mitochondrial oxidative enzymes is obviously one of the causes of higher oxygen consumption by the body, above and beyond the natural increase in consumption

associated with physical activity [10,43]. Adrenergic stimulation of oxidative processes that are not associated with production of useful energy may be another cause [12].

The elevated oxygen demand is covered by activation of respiratory and cardiovascular system functions. Phenylethylamine derivatives increase pulmonary ventilation and heart rate; moreover they cause an additional increase in these indicators when physical loads are imposed [43].

Thus the mechanism of action of these psychostimulants is not based on real expansion of the functional possibilities of the body, such as occurs, for example, in the course of training; instead, it is oriented on maximum, uneconomical use of available possibilities, on "squeezing" them to the limit. This is confirmed, in particular, by the absence of an increase in maximum oxygen consumption in response to the use of these drugs despite the observed increase in physical performance [43]. Maximum oxygen consumption is a universally accepted indicator of aerobic productivity, and one of the most informative ones; its increase is evidence of the body's transition to a higher functional level, at which level, performance is enhanced through structural and functional improvement of the systems supporting physical activity.

Inasmuch as psychomotor stimulants, based on phenylethylamine derivatives, deplete the body, the frequency of their use and of imposing recurrent loads is limited by the time necessary to restore energetic and functional potential after work is done on the backdrop of a preceding administration of the drug. The initial phase of the after-effect period, when depletion of the body's resources is most pronounced, is characterized by additional decline of performance in comparison with normal conditions (when stimulants are not used), and by depression, sluggishness and dystrophy [3,4]. Following use of the most active drugs (phenamine, dexedrine, pervitin), the recovery period may drag on for several days. When recurrent loads are imposed in the presence of noticeable residual fatigue on the backdrop of the use of these drugs, weakening and total disappearance of a positive effect or even a negative influence on performance occurs [6,13,36,42]; moreover this influence intensifies when subsequent loads are imposed with short rest intervals [6].

Such transformation of the effect of these substances from positive to negative is also observed in other complicated conditions when they become more severe, particularly in the presence of hypoxia [5,13] and high ambient temperature [13], which can be explained by the features noted above in the mechanism of action of these drugs—an increase in oxygen demand and elevated heat production. Use of these psychostimulants, with the purpose of enhancing performance, is also undesirable in the presence of pronounced emotional stress, inasmuch as the drugs, which stimulate the sympathetic system, may themselves act as an additional stress factor [18].

On a stress background these substances sharpen the sense of anxiety and mental tension, and worsen psychomotor activity [4,40] to the point of its total breakdown [4]. The more complex the work is, the more negatively the effect of stimulants manifests itself during stress.

The influence of phenylethylamine derivatives on the cardiovascular system, which takes the form of stimulation of the heart and elevation of arterial pressure through sympathomimetic action, is one of the possible unfavorable consequences [2,41]. When myocardial pathology and hypertension are present, severe arrhythmia, stenocardia, myocardial infarction and a hypertensive crisis may develop as a result, especially on the backdrop of physical loads. Consequently, it is dangerous to prescribe these drugs in the presence of such pathology, and caution should also obviously be taken in their use by people in older age groups even without obvious pathology. The greatest caution should be exercised in the use of drugs with pronounced peripheral sympathomimetic action (phenamine, dexedrine, pervitin). It should be emphasized, however, that these same drugs, and phenamine in particular, are among the most effective psychostimulants of this group in terms of their influence on physical performance in uncomplicated conditions [14,15], inasmuch as intensification of cardiac activity facilitates an increase in delivery of oxygen to organs and tissues, and is an important component of the mechanism by which these drugs enhance physical performance.

Pronounced variability of individual effects is one of the shortcomings of psychomotor stimulants based on phenylethylamine derivatives. Even in normal conditions these drugs have a paradoxical action upon 10 - 15 percent of completely healthy people; this action is psychomotor inhibition [4,11]. This is why it would be suitable to test individual sensitivity to these drugs prior to their actual use [11]. D. Davies [21], who briefly summarized experience in studying phenamine in the British army during World War II, noted the pronounced variability of reactions to this drug. According to the author's observations, a normal dose (15 mg) resulted in significant individual differences in the effect of the drug. Moreover it was impossible to predict these differences, and the effects varied from case to case even in the same person. Negative behavior was observed among certain individuals, especially when carrying out complex assignments.

The optimum doses of these drugs vary noticeably depending on the specific conditions [8]. Use of other-than-optimum doses may partially explain cases of absence of a positive effect from the drugs in a number of studies [20].

A significant shortcoming of these drugs is their ability to elicit, other than an elevation of mood, a state of euphoria under which critical perception of reality may break down [34,41]. These drugs elicit euphoria in healthy persons more easily than opium alkaloids and barbiturates [34]. Cases of inadequate behavior may be

explained by a combination of euphoric and toxic action. This action is responsible for the usually observed subjective overstatement of the positive effect of the drugs. The deceptive sensation of noticeably enhanced performance is often accompanied by significantly less pronounced improvement of the objective indicators of activity, or complete absence of any improvement [33,42]. However, weakly expressed euphoria apparently plays a positive role by enhancing positive motivations.

The rapid onset of euphoria is a cause of development of an addiction to psychostimulants based on phenylethylamine derivatives when they are taken repeatedly [31,41]. The most active drugs with the highest lipid solubility—phenamine and pervitin—are the most dangerous in this respect [41]. Addiction is a very serious shortcoming of these drugs, although it is basically of mental and not physical nature [39,41].

The rather narrow range of the therapeutic action of these substances, especially phenamine and pervitin, is one of their shortcomings. Signs of phenamine toxicity manifest themselves at a dose of 30 mg, which is only 1.5 - 3 times the normally employed doses [4]. In complicated conditions, for example in the presence of physical loads, including in combination with high ambient temperature and extreme tiring, toxicity increases noticeably [8,13]. The variability of individual reactions mentioned above promotes manifestation of toxicity in certain cases even when therapeutic doses of phenamine are taken under normal conditions [30].

Toxic effects are observed primarily on the part of the central nervous system, and they are characterized by mental, speech and motor hyperactivity, insomnia, irritability, aggressiveness, a sense of tension and anxiety, headache, and stereotypic motions and acts, for example, continual repetition of the same sentences [17,41]. When latent psychopathology exists, even one-time administration of the strongest-acting drugs may lead to the development of delirium or paranoid psychoses coupled with auditory hallucinations, anxiety, and delirious paranoia [30,31]. Persons with such psychoses present considerable danger. The toxic effects of phenylethylamine derivatives on the periphery manifest themselves primarily through the disturbances of cardiovascular function noted above.

There is another effect inherent to a number of phenylethylamine derivatives (phenamine, dexedrine, pervitin etc.) that may play both a negative and positive role depending on the situation. I am referring to appetite suppression [41]. When work has to be done over the course of many hours and in the absence of the possibility for eating (though, of course, not in the presence of prolonged starvation), the value of this effect is positive, while in the opposite case it becomes negative, particularly during the period of recovery following heavy loads.

Presence of all of the above-described shortcomings of phenamine and pervitin—the first psychostimulants based on phenylethylamine derivatives to be used in the

clinic—encouraged further exploration for drugs among derivatives of this chemical series which would possess these shortcomings to a lesser degree. Such drugs were created. We have now obtained drugs with reduced toxicity and less noticeable peripheral effects, and which elicit habituation and addiction more rarely—pemoline, thozaline, catovit, sidnokarb etc. [1,41]. However, all of the drugs named above are inferior to phenamine and pervitin in expressiveness of stimulatory action on performance in uncomplicated conditions. This is to be expected, inasmuch as the shortcomings of phenylethylamine derivatives are associated predominantly with their principal action, as follows from the cited data.

Actual prescription of particular drugs with the purpose of enhancing performance must account for all possible indications and contraindications in each specific case. The less complicated the conditions of the activity are, the greater the possibilities for using the most active drugs (phenamine, dexedrine and pervitin) and attaining the most significant impact. As the conditions in which work is done become more complicated, it would be suitable to use drugs with milder action, but ones which would be less dangerous from the standpoint of developing undesirable effects. Such drugs can generally be used more widely, and they are preferred over phenamine, dexedrine and pervitin. Thus, while sidnokarb has a weaker influence on performance in normal conditions than phenamine [14], it stimulates the cardiovascular system to a lesser degree, it becomes addictive significantly more rarely, and it depletes the body to a lesser extent [1]. At the same time, the principal negative effects inherent to phenamine are also typical of sidnokarb, though in weakened form: In complicated conditions (emotional stress, overheating etc.) it acts negatively [4,13], it does not allow prolonged use, and it requires individualizing the prescription and strict selection of optimum doses in each specific situation [14].

Completing this survey, we can conclude that psychomotor stimulants based on phenylethylamine derivatives are an effective means of quickly raising and maintaining performance in the presence of relatively simple forms of activity, predominantly in uncomplicated conditions. When the conditions become complicated, these drugs elicit a clear positive effect much more rarely. During work at night (by temporary elimination of the need for sleep) or on the background of pronounced cooling of the body (owing to intensification of heat production by the drugs). When these drugs are to be used, it is always best for subjects to take them preventively before work, while they are still fresh. On the other hand it is extremely difficult to expect a positive impact from the drugs when extreme tiring is developing: Their action would more likely be negative in this case. In the presence of hypoxia and elevated ambient temperature, use of phenylethylamine derivatives must be carefully weighed with regard for the expressiveness of changes that have occurred within the habitat. When significant changes have occurred, use of these drugs is contraindicated. Nor is their prescription suitable in relation to

complex forms of work, inasmuch as the quality of activity may suffer. In cases where work must be done on the backdrop of emotional stress or fear, these drugs should be used, in all probability, only in combination with tranquilizers. It is especially difficult to plan prescription of these drugs in situations characterized by rapid change in the conditions of activity, inasmuch as a dose that was initially optimum might become either ineffective or toxic (for example when an abrupt change occurs in air temperature or oxygen concentration), and even the fact itself of using the drug sometimes begins to play a negative role (with sudden development of emotional stress). Finally, pronounced individual variability of the effects of phenylethylamine derivatives must be kept in mind, and sensitivity to them should be tested beforehand if possible. Use of these drugs must be maximally limited in the presence of cardiovascular pathology and mental instability, and by persons in older age groups. The need for complete rest after working on the backdrop of the action of these drugs, coupled with the corresponding breaks in their use, should be kept in mind. Thus while they are doubtlessly useful in particular situations, phenylethylamine derivatives are characterized by a rather wide range of limitations and contraindications to their prescription as performance-enhancing agents.

Besides phenylethylamine derivatives, psychomotor stimulants also include xanthine derivatives, and primarily caffeine. These drugs have purely secondary significance as performance-enhancing agents, being noticeably inferior to phenylethylamine derivatives [42], but sometimes they may be used jointly with the latter [4]. Psychomotor stimulants of other chemical structure, for example adamantane derivatives, have not yet achieved widespread use.

Bibliography

1. Altshuler, R. A., *EKSPRESS-INFORM, NOV LEKARST. PREPARATY*, No 3, 1976, pp 13-19.
2. Anichkov, S. V., "Neyrofarmakologiya" [Neuropharmacology], Leningrad, 1982.
3. Arushanyan, E. B. and Belozertsev, Yu. A., "Psikho stimulyuyushchiye veshchestva" [Psychostimulatory Substances], Chita, 1979.
4. Vasil'ev, P. V., Belay, V. Ye., Glod, G. D. and Razumeyev, A. N., "Patofiziologicheskiye osnovy aviatsionnoy i kosmicheskoy farmakologii" [Pathophysiological Fundamentals of Aviation and Space Pharmacology], Moscow, 1971.
5. Vinogradov, V. M., Pastushenkov, A. V. and Pastushenkov, L. V., "Farmakologiya dvigatel'noy deyatel'nosti" [Pharmacology of Motor Activity], Moscow, 1969, pp 37-43.
6. Kurochkin, I. G. and Tsikalova, I. S., *FARMAKOI I TOKSIKOI*, Vol 39 No 6, 1976, pp 656-658.
7. Lazarev, N. V., *VOYEN-MOR VRACH*, Vol 2 No 3, 1943, pp 24-28.
8. Lyubimov, B. I. and Ostrovskaya, G. Z., *FARMAKOI I TOKSIKOI*, No 2, 1977, pp 113-136.
9. Morozov, I. S. and Pukhova, G. S., "Farmakologicheskaya regulatsiya protsessov utomleniya" [Pharmacological Regulation of Tiring Processes], Moscow, 1982, pp 102-111.
10. Salnik, B. Yu. and Kapustina, V. A., "Stimulyatory tsentral'noy nervnoy sistemy" [Central Nervous System Stimulants], Tomsk, 1968, Issue 2, pp 75-76.
11. Serevskiy, M. Ya., "Stimulyatory nervnoy sistemy" [Nervous System Stimulators], Moscow, 1943.
12. Skulachev, V. P., "Transformatsiya energii v biomembranakh" [Energy Transformation in Biomembranes], Moscow, 1972.
13. Bobkov, Yu. G., Vinogradov, V. M., Katkov, V. F. et al., "Farmakologicheskaya korrektsiya utomleniya" [Pharmacological Correction of Fatigue], Moscow, 1984.
14. Shashkov, V. S. and Yakota, N. G., *FARMAKOI I TOKSIKOI*, No 2, 1984, pp 5-15.
15. Shashkov, V. S. and Yakota, N. G., *KOSMICHESKAYA BIOI*, No 6, 1980, pp 44-51.
16. Yakovlev, N. N., *FIZIOI ZHURN SSSR*, Vol 56 No 9, 1970, pp 1263-1275.
17. Angrist, B., "Stimulants: Neurochemical, Behavioral and Clinical Perspectives," New York, 1983, pp 1-30.
18. Antelman, S. M. and Chiodo, L. A., "Stimulants: Neurochemical, Behavioral and Clinical Perspectives," New York, 1983, pp 269-300.
19. Barmack, J. E., *J. PSYCHOL*, Vol 5, 1938, pp 128-133.
20. Cooper, D. S., *JAMA*, Vol 222 No 9, 1972, pp 1007-1111.
21. Davies, D. R., *BRIT. MED. BUILL*, Vol 5 No 1, 1947, pp 43-45.
22. Estler, C. J. and Gabrys, M. C., *PSYCHOPHARMACOLOGY*, Vol 60 No 2, 1979, pp 173-176.
23. Gessa, G. L., Clay, G. A. and Brodie, B. B., *LIFE SCI*, Vol 8 No 3, 1969, pp 135-141.
24. Groves, P. M. and Tepper, J. M., "Stimulants: Neurochemical, Behavioral and Clinical Perspectives," New York, 1983, pp 81-130.
25. Heyrodt, H. and Weibenstein, H., "Naunyn-Schmiedeberg's [sic]," *ARCH. EXP. PATH. PHARMACOI*, Vol 195, 1940, pp 273-275.
26. Himms-Hagen, J., *FED. PROC.*, Vol 29 No 4, 1970, pp 1388-1401.

27. Himms-Hagen, J., ANN. REV. PHYSIOL., Vol 38, 1976, pp 315-351.
28. Hollister, L. E., CLIN. PHARMACOL. THER., Vol 10 No 2, 1969, pp 170-198.
29. Kalix, P. and Glennon, R. A., BIOCHEM. PHARMACOL., Vol 35 No 18, 1986, pp 3015-3019.
30. Kosman, M. E. and Unna, K. R., CLIN. PHARMACOL. THER., Vol 9 No 2, 1968, pp 240-254.
31. Kramer, G. C., Fischman, V. S. and Littlefield, D. S., J.A.M.A., Vol 201 No 5, 1967, pp 305-309.
32. Kuczenski, R., "Stimulants: Neurochemical, Behavioral and Clinical Perspectives," New York, 1983, pp 31-62.
33. Kumar, R., ANN. REV. PSYCHOL., Vol 21, 1970, pp 595-621.
34. Lasagna, L., von Felsinger, J. M. and Beecher, H. K., J.A.M.A., Vol 157, 1955, pp 1006-1019.
35. Laties, V. G. and Weiss, B., FED. PROC., Vol 40 No 12, 1981, pp 2689-2692.
36. Smith, G. M. and Beecher, H. K., FED. PROC., Vol 170 No 22, 1959, pp 542-557.
37. Smith, G. M. and Beecher, H. K., FED. PROC., Vol 172 No 14, 1960, pp 1502-1514.
38. Stone, T. W., BRIT. J. PHARMACOL., Vol 56, 1976, pp 101-110.
39. Sulzer, F. and Sanders-Bush, E., ANN. REV. PHARMACOL., Vol 11, 1971, pp 209-230.
40. Valzelli, L., "Psychopharmacology: On Introduction to Experimental and Clinical Principles," New York, 1973.
41. Van Rossum, J. M., INT. REV. NEUROBIOL., Vol 12, 1970, pp 307-335.
42. Weiss, B. and Laties, V. G., PHARMACOL. REV., Vol 14, 1962, pp 1-37.
43. Wyndham, C. H., Rogers, G. G., Benade, A. J. S. and Strydom, B. N., S. AFR. MED. J., Vol 45 No 10, 1971, pp 247-252.

N-5(Hydroxynicotinoyl)-L-Glutamic Acid: Novel Substance With Nootropic Activity

917C0095A Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 53 No 4, Jul-Aug 90 (manuscript received 12 Apr 89) pp 13-16

[Article by T. A. Voronina, T. L. Garibova, I. V. Khromova, Ye. A. Kuznetsova, and L. D. Smirnov, Laboratory of Psychopharmacology, Pharmacology Institute, USSR Academy of Medical Sciences, Moscow]

UDC 615.214.31:547.466.64].076.9

[Abstract] The psychopharmacologic effects of N-5(hydroxynicotinoyl)-L-glutamic acid (nooglutyl-HNA-10), the most active of a number of recently synthesized 5-hydroxynicotinic acid amino acid derivatives with excitatory and inhibitory substituents, were studied on male albino mice (18 - 22 g) and rats (160 - 210 g). Passive avoidance reaction investigations with electrical shock stimuli indicated that HNA-10 in doses of 10 - 100 mg/kg has marked anti-amnesic properties and is superior to piracetam and meclofenoxate and is as effective as aniracetam. Additional research demonstrated that it was the addition of glutamic acid to 3-hydroxypyridine that resulted in the enhancement of the preparation's anti-amnesic properties. HNA-10 in doses of 50, 100, and 400 mg/kg also exhibited anti-hypoxic properties in three different hypoxia models, while the other standard nootropic agents studied had no such effect. In additional studies, the anxiolytic activity of HNA-10 on convulsions, tremors, and hyperkinesia indicated that doses of 50 - 100 mg/kg had no effect in conflict situations, 200 mg/kg prevented convulsions in 16 - 30 percent of animals, and 400 mg/kg eliminated hyperkinesia caused by serotonin. These findings demonstrated that, in addition to anti-amnesic and anti-hypoxic effects, HNA-10 does not disturb conditioned reflex activity and orientation behavior and does not disturb movement coordination. It is hoped that research on the excitatory effect of amino acids on memory genesis and degenerative diseases will lead to treatments and cures for Alzheimer's disease and chronic progressive chorea. Figures 2; tables 1; references 15: 10 Russian, 5 Western.

Chronic Administration of Melatonin Attenuates Effect of Imizine on Dynamics of Forced Swimming and Circadian Rhythms of Movement in Rats

917C0095B Moscow FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian Vol 53 No 4, Jul-Aug 90 (manuscript received 23 Mar 89) pp 16-19

[Article by K. B. Ovanesov, V. A. Baturin, and E. B. Arushanyan, Chair of Pharmacology, Stavropol Medical Institute, Stavropol]

UDC 615.357.814.53.015.2:615.214.32.015.4].076.9

[Abstract] The effects of exogenous melatonin, following its extended administration on imizine activity, was assessed on 84 albino male rats (150 - 180 g) by using models of rhythmic behavioral phenomena that differ in period to understand how the antidepressant effect specifically occurs. The animals were administered imizine (10 mg/kg, intraperitoneally) for 14 days at 9 a.m. each day and melatonin (1 and 10 mg/kg, intraperitoneally) for 7 days at 10 a.m. each day, with daily monitoring of the average duration of immobility and active and passive swimming. The results demonstrated that chronic imizine administration results in shifts in the baseline indices of forced swimming in rats, as indicated by shorter periods of immobilization and longer periods of activity with a decreased number of attempts to escape the tank. In addition, the biorhythmologic index of depression during the day was lower and thus may serve as an indicator of the specific antidepressant activity of the substance. It was also shown that imizine alters the daily movement of the rats, as reflected in increased general motor activity at night. In melatonin experiments, the rats exhibited a slight decrease in movement and some alterations in the rhythmic structure of swimming. Moreover, the depression index fell during the day as measured by the decreasing number of the shortest immobilization cycles. One-time administration of melatonin was shown to have an antidepressant effect. While melatonin itself has no substantial effect on the basic parameters of forced swimming, it does have antagonistic properties when combined with imizine, thereby preventing antidepressant-induced shortening of the immobilization period and extending the active swimming period. Further studies indicated that extended use of melatonin, regardless of the dosage, resulted in alteration of the daily activity of the animals. In addition, regular administration of melatonin and imizine was shown to attenuate shifts in circadian rhythm dynamics caused by the antidepressant. Finally, repeat use of melatonin and the antidepressant resulted in limitation of the biological activity of the preparation in different situations. These findings suggest that the stimulating effect of imizine on motility and the indices

of its specific activity are probably attenuated due to the direct pharmacodynamic interaction of melatonin and the antidepressant in the brain. These data also suggest that the high level of melatonin in psychic depression patients may make some contribution to the organization of pharmacoresistance in antidepressant therapy. Figures 2; references 9; 6 Russian, 3 Western.

Analgesic Activity of Coordination Compounds of Methionine-Enkephalin and Bivalent Metals

917C0095C Moscow *FARMAKOLOGIYA I TOKSIKOLOGIYA in Russian* Vol 53 No 4, Jul-Aug 90 (manuscript received 21 Jun 89) pp 24-25

[Article by L. A. Gromov and E. A. Serdyuk, Psychopharmacology Laboratory, Kiev Pharmacology and Toxicology Scientific Research Institute, Kiev]

UDC 615.212.7:547.95:547.943].012.1

[Abstract] The potential for obtaining more stable analgesics by developing coordination compounds of enkephalins with transitional metals was investigated in view of the fact that analgesic enkephalins are superior to existing narcotic agents. Coordination compounds of methionine-enkephalin were made with cobalt, nickel, copper, and zinc, and their analgesic activity was compared with that of native methionine-enkephalin, morphine, and promedole in studies involving 18 - 25 g mice. The results demonstrated that coordination compounds of methionine-enkephalin and copper were the most effective. Subsequent studies involving acetylcholine action on the isolated membrane of dialyzed neurons of the central nervous system in the *Helix pomatia* demonstrated that the enhanced activity of methionine-enkephalin coordination compounds was due to the formation of a stronger bond with the opiate receptors, thereby making the latter less accessible to enkephalinase action. These findings indicate the potential for using coordination compounds of methionine-enkephalins to reduce toxicity while enhancing its pharmacological effectiveness. Figures 1; tables 1; references 4; 2 Russian, 2 Western.

Audiogenic Reactions of Rats Following Ultraviolet Radiation of Their Eyes

917C0097F Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 24 No 4, Jul-Aug 90 (manuscript received 20 Feb 89) pp 36-38

[Article by G. V. Lobacheva]

UDC 612.858.73.06:612.84.014.44:52-739

[Abstract] The effects of ultraviolet radiation of the eyes (LOS-2 apparatus, 290 - 310 nm) on the central nervous system (CNS) were assessed on female Wistar rats (222 g). A 96 decibel (90 sec) sound irritant was employed to induce an epileptic-like seizure in the animals. The temporal and strength parameters and nature of the rodent reactions to the audiogenic stimulus make it possible to judge the ratio of excitatory and inhibitory processes in the CNS, and thus assess the functional condition of the CNS. The results demonstrated that there was no connection between sound sensitivity and the degree of corneal opacification. An analysis of various indices of convulsant activity suggested that there is a general tendency to enhance the inhibitory and depress the stimulatory processes of the CNS as a result of increased ultraviolet radiation doses. It was demonstrated that the sound stimulus passes through a number of subcortical formations, reaches the cortical stimulus of the auditory analyzer, and leads to widespread irritation of the stimulus process in cerebral neurons, thereby inducing convulsions. The findings suggest that weakening of convulsant activity can occur due to a decrease in the number of afferent impulses to the CNS from the peripheral section of the visual analyzer. Thus, structural changes in the eyes that occur as a result of increasing doses of ultraviolet radiation may lead to functional disorders that are associated with enhancing the inhibitory processes in the CNS. Figures 1; tables 1; references 11; 10 Russian, 1 Western.

Superslow EEG Oscillations and Velocity Correlates of Problem Solving

917C0102A Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 16 No 7, Jul-Aug 90 (manuscript received 16 May 88) pp 21-25

[Article by G. A. Aminev and A. R. Kudashev, Bashkir State University, Ufa]

UDC 612.821.1+612.821.3

[Abstract] The involvement of superslow EEG waves in intellectual processes was investigated in a group of 41 students with a mean age of 24.5 years, employing a series of tasks equivalent to the 'game of 5' [sic] [Pushkin, V. N., Psikhologiya i Kibernetika (Psychology and Cybernetics), Moscow, 1971]. Analysis of the visual-motor demonstrated that fluctuations in reaction times were most clearly reflected in the EEG components with

a periodicity of 20 sec. In addition, a positive correlation was observed to prevail between the 14 - 32 sec patterns and the rate at which equivalence algorithms were reached. A similar relationship was shown to apply to 1.5 - 2.5 min periodicities and stereotypy in solution of homomorphic problems. Tables 1; references 14; 11 Russian, 3 Western.

Physiological Dynamics of Monotonous Operation 1.5 h in Duration

917C0102B Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 16 No 7, Jul-Aug 90 (manuscript received 15 Aug 88) pp 158-161

[Article by Yu. G. Grigoryev, S. N. Lukyanova, V. P. Makarov, V. P. Nazarov, N. G. Gorban, V. Yu. Selkova and A. I. Pechenikhin, Institute of Biophysics, USSR Ministry of Health, Moscow]

UDC 612.741.1

[Abstract] The physiological status of 29 male subjects, 25 - 40 years old, was assessed in relation to a 1.5 h monotonous operational assignment. The assignment consisted of circular point tracking on a television screen under conditions of partial sensory (visual, auditory) deprivation. The results demonstrated that an assignment of this type, lacking emotional and intellectual components, was accomplished without significant physiologic alterations. Nevertheless, a tendency toward inhibitory processes in the CNS became evident and reflected individual capacity for performance under monotonous conditions. The EEG α band was confirmed to be the key indicator of occupational fitness under these conditions and, consequently, of individual typology. Tables 3; references 7; 6 Russian, 1 Western.

Temporal Factors in Psychophysiological Adjustments of Information Systems Experts

917C0102C Moscow FIZIOLOGIYA CHELOVEKA in Russian Vol 16 No 7, Jul-Aug 90 (manuscript received 18 Apr 88) pp 164-167

[Article by A. P. Shulga and S. V. Guskov, Scientific Research Institute of Normal Physiology imeni P. K. Anokhin, USSR Academy of Medical Sciences, Moscow]

UDC 612.821.3:57.034

[Abstract] An analysis was conducted on psychophysiological adjustments of 45 military 'operators', the male subjects ranging in age from 25 - 45 years, to assess the sequelae of working conditions. The results demonstrated that within a work week, highest stress is encountered at the beginning of the week and in the case of shift work, the night shift is most stressful. Within the framework of a diurnal cycle, the evening hours and the first half of a night shift represent the most stressful situations. Onset of positional fatigue, due to hypokinesia, toward the end of a shift leads to imbalance in the

cardiopulmonary system manifested in a reduction in the stroke volume/heart rate index. Concomitant mental fatigue resulted in an increase in the oxygen utilization coefficient, which showed direct correlation with the intensity of the intellectual effort involved. Figures 1; tables 1; references 10; Russian.

Determination of Informational Load in Operators

917C0102D Moscow FIZIOLOGIYA CHELOVEKA
in Russian Vol 16 No 7, Jul-Aug 90 (manuscript
received 28 Jan 89) pp 173-174

[Article by O. Yu. Netudykhatka, V. N. Yevstafyev, V. G. Kravets and G. Ye. Palatnik, All-Union Scientific Research Institute of Hygiene of Water Transportation, USSR Ministry of Health, Odessa]

UDC 612.015.002.6:612.766.1

[Abstract] Cursory description is provided on a device (USSR author's certificate No. 1395290) for measuring informational load that was tested against selected physiological parameters in the case of marine and river navigators. The device provides data in the form of total angles of deviation (TAD) per unit of time in tracking a moving target. The coefficient of correlation between TAD and changes in selected physiological parameters was as follows: $r = +0.97$ for heart rate, $+0.87$ for Bayevskiy stress index, and $+0.67$ for urinary epinephrine. Accordingly, the device has been shown to be a reliable and rapid means of assessing possible job-related informational overload. Figures 1; tables 1; references 4; Russian.

Physiologically Active Substances

917C0115A Kiev FIZIOLOGICHESKI AKTIVNYE
VESHCHESTVA. TOM 21. in Russian 1989 (Signed to
press 20 Oct 89) pp 0, 64-68, 68-74, 99-102

[Annotation, two articles and synopses from book
"Physiologically Active Substances"]

[Text] Annotation

This collection examines synthesis of organic and organo-elemental compounds containing nitrogen, sulfur, phosphorus and halogens, and synthesis of analogues of natural and medicinal compounds. The results of studying the antimicrobial, antihemorrhagic, cholinesterase, antiviral and antitumor properties and pesticidal and growth-regulating action are described.

This book is intended for workers of scientific research institutions and higher educational institutions, and specialists of a chemical, biological, agricultural or medical profile.

"Herbicidal Activity of Dibenzo-18-Crown-6 and Its Derivatives," by Yu. G. Merezhinskiy, V. V. Shvartau, Yu. P. Fedorenko, L. M. Tochilkina and T. N. Kudrya, Plant Physiology Institute and Organic Chemistry Institute, UkSSR Academy of Sciences, Kiev.

UDC 632.954+547.26.118

The possibility described in the literature for using macrocyclic compounds (crown ethers) to create "containerized" drugs better able to penetrate epidermal cell membranes is interesting from the aspect of creating new herbicides and regulating the phytotoxicity of known ones. Thus, it was demonstrated that 15-crown-5 significantly raises the phytotoxicity of eptam, trellan, dual and 2,4-D [3,4]. In the opinion of the authors of [5], when herbicides are used jointly with a polyether, their phytotoxic action is amplified owing to acceleration of the herbicide's transportation through the plasmalemma of plant cells. The highly lipophilic nature of macrocyclic complexes, and particularly of crown ethers, is known as well. This property allows these compounds to penetrate the cell, surmounting the barrier created by the epidermal membrane with varying degrees of ease. "Facilitated" uptake by the cell and accompanying changes in the structure and properties of cell membranes [5,7] make it possible to hypothesize that these compounds have potential phytotoxicity which is realized at the level of the photosynthetic apparatus of plants. In this connection, there is interest in studying the herbicidal activity of crown ethers not only on the basis of the commonly accepted methodology [9], but also by evaluating the action of the compounds upon the photosynthetic apparatus of plants.

This paper is devoted to a study of the phytotoxicity of dibenzo-18-crown-6 and its derivatives in relation to mono- and dicotyledons. The action of the preparations upon plants was assessed by Sergeyeva's procedure [9]. Sprouts were obtained in Petri dishes on agar medium containing a certain quantity of the compound under investigation. Pure agar was used as the control. The herbicides eptam, TCA and lenacil were used as the standards. The results are shown in Table 1. The data were subjected to statistical treatment by Dospekhov's method [1]. The error of the arithmetic mean was within 1 - 3.2 percent.

Table 1. Results of Initial Tests (Percent of Control Sprouts)

No	Crown Ether	Concentration, %	Length of Plant Parts				Germination Rate	
			Barley		Radish		Barley	Radish
			Root	Stem	Root	Stem		
1	Dibenzo-18-crown-6	0.01	42	47	48	50	80	80
		0.001	64	77	57	87	93	87
		0.0001	102	93	93	94	96	88
2	Cis-dinitrodibenzo-18-crown-6	0.01	56	56	46	36	82	104
		0.001	87	93	102	60	88	106
		0.0001	87	93	117	81	105	100
3	Trans-dinitrodibenzo-18-crown-6	0.01	38	50	41	58	82	100
		0.001	65	90	85	57	94	102
		0.0001	70	93	109	64	100	107
4	diaminodibenzo-18-crown-6	0.01	35	58	47	74	82	93
		0.001	65	83	72	84	100	102
		0.0001	73	92	77	115	100	100
5	Phosphorylated cis-diamino-DB-18-c-6	0.01	52	74	70	96	94	92
		0.001	57	77	76	102	96	105
		0.0001	75	80	104	114	96	104
6	Adamantyl-1-phosphonyl-dibenzo-17-c-6	0.01	54	63	97	103	78	89
		0.001	57	58	94	100	79	86
		0.0001	64	65	98	110	79	86
7	Phosphorylated diamino-DB-18-c-6	0.01	83	92	92	104	100	97
		0.001	84	96	99	98	101	97
		0.0001	89	100	97	114	101	101
8	Eptam (S-ethyl-N,N-dipropylthio-carbamate)	0.001	0	0	6	8	0	12
		0.0001	0	2	24	34	2	45
9	TCA (sodium trichloracetate)	0.001	69	71	91	96	82	102
		0.0001	74	75	103	105	91	103
10	Lenact (3-cyclohexyl-5,6-trimethyluracil)	0.001	14	18	5	3	77	10
		0.0001	34	37	17	13	91	73

The action of the compounds upon the photosynthetic system was assessed by the fluorescence induction (FI) method, which reflects the kinetics of the fluorescence yield of photosynthesizing organisms in the first minutes after they are transferred from darkness to light. The stages of FI were identified as follows in the study of the action of the compounds upon the kinetics of variable fluorescence: 0—initial level, 1—first maximum (observed after 0.01 - 0.1 sec depending on light intensity and sample characteristics), D—intermediate decline, P—second maximum (observed after 0.5 - 5 sec), S—intermediate stationary level, M—third maximum (on the order of tens of seconds) and T—terminal stationary level. According to [2], the fluorescence yield of green plants is determined by the oxidation-reduction state of the primary electron acceptor of photosynthetic system II. The upward trend 0 - 1 is a purely photochemical process in the case where photochemical reactions are inhibited by a disconnector. Thus, the rate of growth of the intensity of fluorescence, in approximately the 50

msec region, serves as an indicator of the proportion of inhibited ETTs (electron transport centers). The upward trend D-P [6] is evoked by accumulation of the primary electron acceptor of photosynthetic system I in a reduced state. In this connection, the rate of growth of the intensity of fluorescence in this region may serve as a criterion for the proportion of uninhibited ETTs in the sample in question. The rate of decline of P-S depends to a significant degree on appearance of a pH gradient on the thylakoid membrane, and it is thus associated with the rate of phosphorylation.

Fluorescence was excited in the experiments by radiation from a DRSh-250-2 arc lamp, passed through an SZS-3 (2 mm) filter and a 2-centimeter water filter containing 2 percent CuSO_4 solution. Observations were made through KS11 and KS14 filters by means of an MDR-2 monochromator in the 685 nm region using a 2 mm slit. The shutter open time and the time constant of the receiving-amplifying channel were 1 msec. Fluorescence induction curves were recorded by means of an

S8-13

general-purpose recording oscillograph in three ranges—50 msec/division, 500 msec/division and 1 sec/division. Diuron, lenacil and pyramine were used as the standard disconnectors. The results are shown in Table 2.

Table 2. Effect of Dibenzo-18-Crown-6, Its Derivatives and Herbicides on the Rate of Photosynthetic Electron Transport (I) and Photophosphorylation (II)

Crown Ether (0.01%), Herbicide	Radish		Barley	
	I	II	I	II
	% of Control			
1	43	54	-	-
2	45	82	71	35
3	78	119	88	90
4	102	124	99	102
5	77	67	60	66
6	55	64	-	-
7	103	60	84	88
Diuron 10^{-5} M	2	0	0	0
Eptam 5×10^{-5} M	115	78	92	79
Pyramine 10^{-4} M	6	0	10	0
Lenacil 10^{-5} M	0	0	66	84

I—The rate of photosynthetic electron transport was defined as $(F(P)-F_0)/F_0$.

II—Photophosphorylation was determined from rate P of the decline of the induction curve.

As is evident from Table 1, DB-18-c-6 at a concentration of 0.01 - 0.001 percent weakly inhibits growth of mono- and dicotyledons; at a concentration of 0.0001 percent, it weakly stimulates root formation in barley. The position of the introduced nitro groups significantly affects the phytotoxicity of the crown ether: Nitro groups in cis position (compound 2) weaken the phytotoxicity of DB-18-c-6 to barley and somewhat amplify it to the radish; in the trans position (compound 3) we observe the reverse effect: An increase in the compound's phytotoxicity to barley. Mention should be made of the increase in germination rate of radishes treated with both cis- and trans-dinitro-DB-18-c-6. Replacement of nitro groups by amino groups increases selectivity (compound 4), leading to predominant inhibition of growth and germination of barley. Phosphorylation of diamino-DB-18-c-6 weakens the latter's phytotoxicity. As with compounds 4 and 5, compounds 6 and 7 are more active in relation to cereal grasses.

Comparison of the activity of DB-18-c-6 and its derivatives with the action of eptam and lenacil reveals that the phytotoxicity of the series in question is low, manifesting itself in the stages of germination and initial plant growth. Mention should be made of weak stimulation of sprouting (compounds 2, 3, 5) and initial growth of

sprouts (compounds 2, 3, 4, 5, 6, 7), of the radish predominantly, in response to low concentrations of crown ethers, which is consistent with the growth-regulating properties of the series demonstrated earlier [8]. The action of these compounds upon photosynthetic processes manifests itself differently (see Table 2).

Table 3. Features of the Joint Action of Dibenzo-18-Crown-6 and Its Derivatives With Eptam

Crown Ether	Concentration, %	Eptam 0.0002%	
		Radish	Barley
1	0.01	+	+
2	0.01	-	-
3	0.01	+	-
4	0.01	-	H
5	0.01	+	+
6	0.01	+	+

Note: The plus symbol indicates intensification (the minus symbol indicates weakening) of the phytotoxic action of eptam in joint application with the crown ether. H—the activity of the herbicide remains unchanged. The mixture's activity was evaluated on the basis of changes in plant growth.

It is evident from Table 2 that DB-18-c-6 suppresses both electron transport and photophosphorylation. The action of some of its derivatives is interesting: compound 2 significantly inhibits photophosphorylation in barley, and blocks it weakly in the radish and compounds 3 and 4 stimulate photophosphorylation in the radish, while not changing in barley. The unique features of the action of these compounds makes it possible not only to find highly active herbicides, photosynthetic herbicides primarily, but also to modify the herbicidal activity of known preparations. The results shown in Table 3 reveal that it is possible to regulate the toxicity of the herbicide eptam by using it jointly with crown ethers of the series in question.

Thus, in addition to their low phytotoxicity in relation to mono- and dicotyledon sprouts, dibenzo-18-crown-6 and its derivatives possess potential phytotoxicity at the level of the plant's photosynthetic system, and they are effective in raising the activity of known herbicides. Further study of the properties of this class would be of interest both from the aspect of finding new highly active herbicides and in terms of creating complex preparations, expanding the possibilities of utilizing herbicides already in use in agricultural production.

Bibliography

1. Dospekhov, B. A., "Metodika polevogo opyta" [Procedures of the Field Experiment], Moscow, Agropromizdat, 1985, p. 351.
2. Karapetyan, N. V., "Variable Fluorescence of Chlorophyll During Photosynthesis," USPEKHI SOVREM. BIOLOGII, Vol. 83 No. 3, 1977, pp. 370-386.
3. Author's Certificate No 1045874 USSR, A 01 N 31/02, "A Method of Controlling Weeds," N. S.

Kravchenko, A. V. Bogatskiy, V. V. Mily, N. G. Lukyanenko; published 7 October 1983, Bulletin No 37

4. Author's Certificate No 1045875 USSR, A 01 N 31/18, "A Method of Controlling Weeds," N. S. Kravchenko; published 7 October 1983, Bulletin No 37

5. Lukyanenko, N. G., Bogatskiy, A. V. and Nazarov, Ye. I., "Raising the Herbicidal Activity of Eptam by Means of 15-Crown-5," FIZIOLOGIYA I BIOKHIMIYA KULTUR RASTENIY, Vol 17 No 5, 1985, pp 497-501

6. Matorin, N. N., Venediktov, A. V. and Rubin, A. B., "Delayed Fluorescence and Its Use to Evaluate the State of a Plant Organism," IZV. AN SSSR. SER. BIOL., No 4, 1985, pp 508-520

7. Ovchinnikov, Yu. A., Ivanov, V. T. and Shkrob, A. M., "Membranoaktivnyye kompleksoy" [Membrane-Active Complexones], Moscow, Nauka, 1974, p 462.

8. Reydalova, L. I., Kudrya, T. N. and Tochikina, L. M., "Growth Regulating Activity of Dibenzo-18-Crown-6 and Its Derivatives," FIZIOLOGICHESKI AKTIV VESHCHESTVA, No 17, pp 41-45.

9. Sergeyeva, T. A., "Procedures of Laboratory Herbicide Testing," ZASHCHITA RASTENIY, No 2, 1963, pp 42-43.

"Investigation of the Interaction of O-Phosphorylated Oximes With Homeotherm Esterases.

The Role of Esterases in Toxicity," by G. F. Makhayeva, V. L. Yankovskaya, L. M. Kochetova, B. K. Beznosko, V. B. Sokolov, V. K. Brel, V. V. Malygin and I. V. Martynov, Institute of Physiologically Active Substances, USSR Academy of Sciences.

UDC 547.26.118:577.152.311.042:541.697+519.237.5

World production of organo-phosphoric pesticides is nearing 200,000 tons per year, and they continue to occupy first place among other classes of pesticides in scale of use in agriculture [1]. The intensity with which new organo-phosphoric pesticides possessing high effectiveness and selective action are being sought is not declining. In this case, the hygienic aspects of using organo-phosphoric pesticides are becoming extremely significant, and in a number of cases, decisive to plant protection. This imposes higher requirements on studying the toxicology of organo-phosphoric pesticides in experimental conditions, especially when the discussion turns to new classes of potential pesticides.

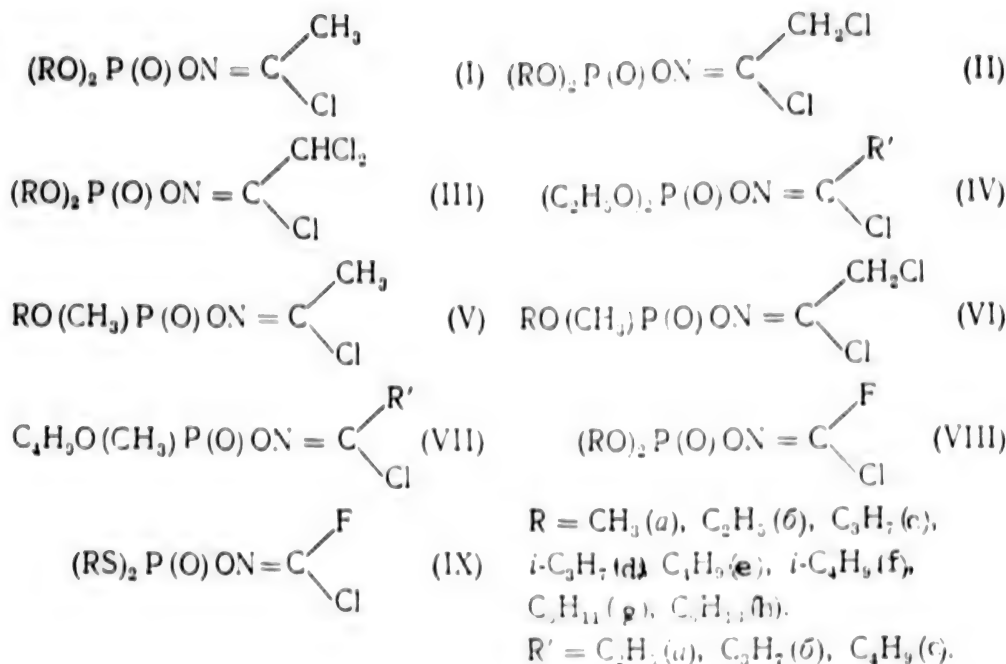
Besides their specific anti-acetylcholinesterase (anti-ACE) activity, biochemical processes occurring with the

compound at the toxic-kinetic stage—that is, along the path toward the biological target, acetylcholinesterase (ACE)—goes a long way in determining the toxicity of organo-phosphoric pesticides [2]. These processes include metabolic transformations of organo-phosphoric pesticides, occurring with the participation of oxidases of mixed function, glutathione-S-transferase and aryl- and carboxylesterases, and leading to both activation and detoxification of xenobiotics [3,4], as well as phosphorylation of nonspecific esterases, carboxylesterase (CE) and butyrylcholinesterase (BuCE), which leads to expenditure of the substance in the toxic-kinetic stage, and reduction of its effective concentration at the biological target [5,6]. In this case, these enzymes act as "points of loss" of organo-phosphoric pesticides in the organism, and interaction with them has a significant effect on the toxicity of organo-phosphoric pesticides.

It appears suitable to utilize an integrated approach to studying the biochemical mechanisms responsible for development of the toxicity of organo-phosphoric pesticides, and especially of new compounds. Such an approach might include, in addition to determining the acute toxicity of the compounds, assessment of their interaction with the principal biotarget—ACE, and with enzymes, or "points of loss"—CE and BuCE, and study of the role of metabolic transformations of organo-phosphoric pesticides along the path to the biotarget. Use of QSAR methods to analyze the relationship between structural and antienzymatic activity makes it possible to reveal factors determining the effectiveness of interaction of organo-phosphoric pesticides with ACE and enzymes serving as "points of loss." Joint analysis of the obtained data makes it possible to more clearly formulate the requirements on organo-phosphoric pesticide structure ensuring low toxicity of the pesticides to homeotherms, and it indicates the ways of regulating toxicity both at the stage of interaction between the organo-phosphoric pesticide and ACE, and in the toxic-kinetic stage.

Having the goal of investigating the biochemical mechanisms behind development of the toxicity of O-phosphorylated oximes (I-IX) synthesized as potential pesticides [7,8], this paper studies their interaction with the esterases of homeothermic animals.

The kinetics of inhibition of ACE, BuCE and CE by compounds I-IX were studied in experiments with enzymatic preparations. It was established that all of the compounds studied irreversibly block these enzymes. Antienzymatic activity was evaluated from the magnitude of the bimolecular rate constant (k^1) for interaction of the compounds with the enzyme. The obtained values of K^1 are shown in the table.



Bimolecular Rate Constants for Inhibition ($\text{k}^{\text{II}}\text{M}^{-1}\text{min}^{-1}$) of ACE in Human Erythrocytes, BuCE in Horse Serum and CE in Pig Liver by O-Phosphorylated Oximes

Compound	R or R'	$\text{k}^{\text{II}}\text{M}^{-1}\text{min}^{-1}$		
		ACE	BuCE	CE
Ia	CH_3	1.10×10^{-4}	3.86×10^{-3}	9.15×10^{-3}
Ib	C_2H_5	4.39×10^{-3}	$4.0-7 \times 10^{-4}$	4.06×10^{-4}
Ic	C_3H_7	2.29×10^{-3}	$1.2-6 \times 10^{-5}$	7.80×10^{-5}
Ie	C_4H_9	2.94×10^{-3}	$5.1-5 \times 10^{-4}$	8.45×10^{-6}
If	$i\text{-C}_4\text{H}_9$	2.73×10^{-3}	9.80×10^{-4}	7.60×10^{-6}
Ig	C_5H_{11}	1.23×10^{-4}	$2-00 \times 10^{-5}$	-
IIa	CH_3	1.06×10^{-3}	1.34×10^{-3}	4.74×10^{-5}
IIb	C_2H_5	6.81×10^{-4}	$1-74 \times 10^{-6}$	5.41×10^{-6}
IIc	C_3H_7	1.77×10^{-5}	$1-49 \times 10^{-7}$	5.01×10^{-7}
IIf	C_4H_9	1.16×10^{-6}	$7-08 \times 10^{-7}$	3.25×10^{-8}
IIg	$i\text{-C}_4\text{H}_9$	7.87×10^{-5}	7.90×10^{-7}	1.20×10^{-8}
IIg	C_5H_{11}	8.10×10^{-5}	$1-59 \times 10^{-8}$	-
IIIa	CH_3	5.19×10^{-3}	1.52×10^{-6}	-
IIIb	C_2H_5	1.27×10^{-3}	$9-84 \times 10^{-6}$	7.33×10^{-7}
IIIc	C_3H_7	7.05×10^{-3}	$1-77 \times 10^{-8}$	-
IIIe	C_4H_9	2.45×10^{-6}	$1-84 \times 10^{-8}$	-
IIIg	C_5H_{11}	3.01×10^{-6}	-	-
IVa	C_2H_5	2.93×10^{-3}	$2-42 \times 10^{-4}$	1.53×10^{-4}
IVb	C_3H_7	4.29×10^{-3}	$2-22 \times 10^{-4}$	4.59×10^{-3}
IVc	C_4H_9	5.99×10^{-3}	$1-07 \times 10^{-5}$	1.21×10^{-4}
Vb	C_2H_5	2.07×10^{-3}	$7.3-4 \times 10^{-2}$	1.15×10^{-3}
Vc	C_3H_7	3.11×10^{-3}	$1.0-4 \times 10^{-4}$	3.90×10^{-3}
Vd	$i\text{-C}_3\text{H}_7$	8.50×10^{-4}	3.96×10^{-5}	4.07×10^{-4}
Ve	C_4H_9	8.50×10^{-3}	$8-28 \times 10^{-4}$	4.12×10^{-4}
Vg	C_5H_{11}	2.90×10^{-4}	$8-20 \times 10^{-4}$	3.50×10^{-4}

Bimolecular Rate Constants for Inhibition ($k^{\text{II}} \text{M}^{-1} \text{min}^{-1}$) of ACE in Human Erythrocytes, BuCE in Horse Serum and CE in Pig Liver by O-Phosphorylated Oximes (Continued)

Compound	R or R'	$k^{\text{II}} \text{M}^{-1} \text{min}^{-1}$		
		ACE	BuCE	CE
Vh	C_6H_{13}	9.98×10^4	1.54×10^5	2.90×10^4
Vlb	C_2H_5	2.12×10^5	3.75×10^5	3.16×10^6
Vlc	C_3H_7	1.23×10^6	3.87×10^6	3.09×10^6
Vle	C_4H_9	3.50×10^6	2.98×10^7	1.56×10^7
Vlla	C_2H_5	4.60×10^3	8.40×10^4	2.90×10^4
Vllb	C_3H_7	4.60×10^3	1.59×10^5	1.03×10^4
Vllc	C_4H_9	8.70×10^3	4.56×10^5	2.12×10^4
Vllla	CH_3	5.80×10^4	4.19×10^4	1.79×10^5
Vlllb	C_2H_5	1.86×10^5	1.25×10^6	7.71×10^5
Vlllc	C_3H_7	1.51×10^5	6.00×10^6	2.12×10^6
Vllle	C_4H_9	1.97×10^5	3.86×10^7	6.12×10^7
Vlllg	C_5H_{11}	9.87×10^5	2.06×10^7	1.34×10^8
IXb	C_2H_5	8.16×10^5	1.87×10^6	1.46×10^7
IXc	C_3H_7	1.17×10^6	7.59×10^6	6.88×10^7
IXe	C_4H_9	1.70×10^6	1.90×10^7	
IXf	<i>i</i> - C_4H_9	1.26×10^6	1.04×10^7	
IXg	C_5H_{11}	1.22×10^6	1.45×10^6	9.20×10^7

It is evident from the table that phosphates I and IV are weak irreversible inhibitors of ACE; introduction of one (II) and two (III) atoms of chlorine into the alkylchloroformoxime outgoing group leads to significant growth of antiesterase activity in relation to all three enzymes. Compounds VIII with a fluorine atom in the oxime outgoing group possess anti-ACE activity close to the activity of II, which contain a halogen-methyl fragment; in this case, they are significantly inferior to the latter in their anticholinesterase and antituberculinesterase activity. The higher antiesterase activity of dialkylthiolphosphates IX in comparison with phosphates VIII stems from the "thiol effect" of S-alkyl groups [9].

When we go on from phosphates I to the corresponding methylphosphonates V, we observe an increase in anti-ACE activity; in this case, activity in relation to CE and BuCE decreases—to a lesser degree for BuCE and to a significantly greater degree (by one to two orders of magnitude) for CE. Growth of antiesterase activity, occurring as we go from compounds I to II in the case of $\text{R} = \text{C}_3\text{H}_7$ (for example $k^{\text{II}}(\text{CH}_2\text{Cl}) / k^{\text{II}}(\text{CH}_3)$ for ACE is approximately 100), is difficult to explain by differences in their phosphorylating capability, inasmuch as the constants for alkaline hydrolysis of Ic and Ilc are correspondingly 0.014 and 0.023 min^{-1} (pH 9.0, 25°C). It is more probable that the high inhibitory capability of compounds II in comparison with I stems from more effective binding by II in the active center of the enzyme at the stage of formation of the enzyme-inhibitor complex.

The prospects of quantitative analysis of the relationship between structural and antiesterase activity of organophosphoric compounds was demonstrated earlier in [10-12] with the example of *bis*-phosphorylated methanes

and dialkyl (α -carbomethoxy- β,β,β -trifluoroethyl) phosphates. Using the models of Hansch and Kubini [transliteration], it was established that hydrophobic interactions play a more significant role in inhibition of CE and BuCE, as compared to ACE. This paper investigates the dependence between the inhibition rate constants k^{II} and the hydrophobic constants of alkyl substituents calculated by Hansch's method [13]. The linear segments of curves passing through the maximum were examined. The dependence of $\lg k^{\text{II}}$ on hydrophobicity is described well in the cases under examination by the linear equations

$\lg k^{\text{II}}_{\text{CE}} = 2.726 + 1.076\Sigma\pi \text{ (I)},$	$n = 5, r^2 = 0.967,$	(1)
$\lg k^{\text{II}}_{\text{BuCE}} = 4.369 + 0.898\Sigma\pi \text{ (II)},$	$n = 5, r^2 = 0.989,$	(2)
$\lg k^{\text{II}}_{\text{CE}} = 4.893 + 0.900\Sigma\pi \text{ (II)},$	$n = 5, r^2 = 0.934,$	(3)
$\lg k^{\text{II}}_{\text{ACE}} = 4.554 + 0.248\Sigma\pi \text{ (VIII)},$	$n = 5, r^2 = 0.785,$	(4)
$\lg k^{\text{II}}_{\text{BuCE}} = 3.877 + 0.959\Sigma\pi \text{ (VIII)},$	$n = 4, r^2 = 0.967,$	(5)
$\lg k^{\text{II}}_{\text{CE}} = 4.384 + 0.766\Sigma\pi \text{ (VIII)},$	$n = 4, r^2 = 0.958,$	(6)
$\lg k^{\text{II}}_{\text{ACE}} = 1.875 + 0.866\Sigma\pi \text{ (V)},$	$n = 5, r^2 = 0.971,$	(7)

The magnitudes of the coefficients of $\Sigma\pi$ in equations 1 - 7 make it possible to evaluate the role of hydrophobic interactions in the course of esterase inhibition by O-phosphorylated oximes. In the case of CE and BuCE, coefficients of $\Sigma\pi$ close to unity in equations (1)-(3), (5), (6) indicate that hydrophobic interactions make the dominant contribution to inhibition of these enzymes by phosphates I-III and VIII. The dependence of anticholinesterase activity on hydrophobicity is less pronounced, and it is determined by the structure of the

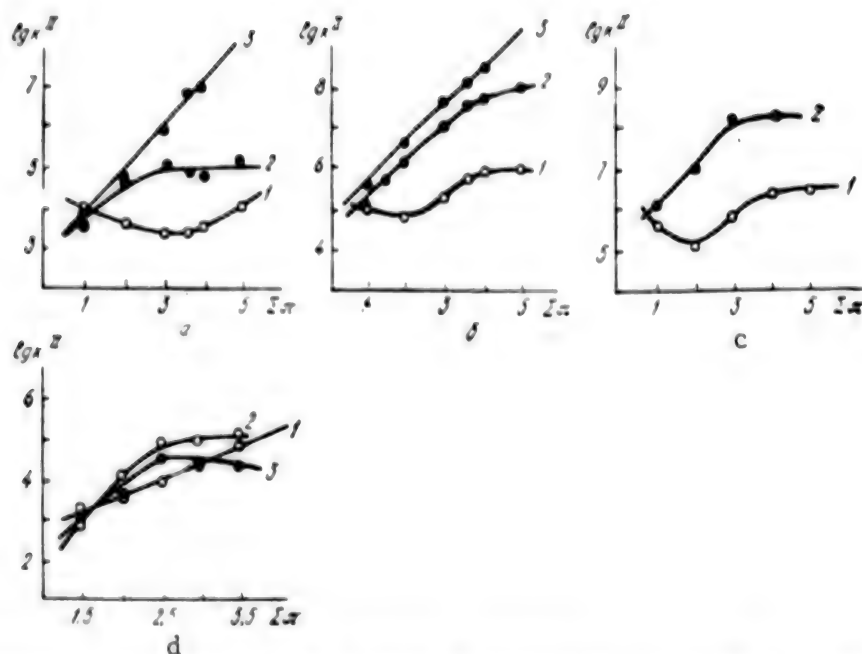


Figure 1. Dependence of the Logarithms of the Constants of Inhibition of ACE (1), BuCE (2) and CE (3) by Compounds I (a), II (b), III (c) and V (d) on Hydrophobicity of Alkyl Radicals

outgoing group (Figure 1 a-c, Figure 2). Change in the nature of the dependence $\lg k'' = f(\Sigma\pi)$ in response to substitution of CH_3 by CH_2Cl (II) and CHCl_2 (III) (Figure 1 a-c) is apparently the product of change in orientation of the inhibitor's molecule in the active center of ACE, which is an indication that the alkylchloroformoxime group takes part in the binding of the inhibitor molecule in the enzyme's active center. It is interesting that when the halogen-methyl group (phosphates I-III) is substituted by F (phosphates VIII), anti-ACE activity grows linearly with growth of the hydrophobicity of the compounds (Figure 2a). However, in this case, the coefficient of $\Sigma\pi$ is significantly less than 1

(equation 4), which indicates that hydrophobic interactions play a less significant role.

As is evident from Figure 1d, in the case of methylphosphonates V, in contrast to the corresponding phosphates (1, Figure 1a), anti-ACE activity grows linearly with increasing length of the O-alkyl radical, and the nature of the dependence does not change when one atom of chlorine is introduced into the molecule (methylphosphonates VI)—a property resulting from the fact that the methylphosphonate grouping is more complementary to the active surface of ACE. Of interest is the high coefficient of $\Sigma\pi$ in equation 7, close to 1. However, as is evident from Figure 1d, when it comes to inhibition by methylphosphonates the contribution of hydrophobic interactions is significantly higher in the case of CE and BuCE than in the case of inhibition of ACE.

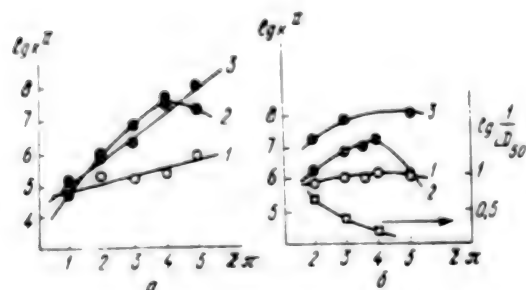


Figure 2. Dependence of the Logarithms of the Constants of Inhibition of ACE (1), BuCE (2) and CE (3) by Compounds VIII (a), IX (b) and of the Acute Toxicity of Compounds IX (c) on Hydrophobicity of Alkyl Radicals

Preferential binding of phosphates I-III, VIII, IX, with enzymes acting as "points of loss", which is especially pronounced as the length of O-alkyl radicals increases (Figure 1 a-c, Figure 2) and the absence of this effect in the case of methylphosphonates V (Figure 1d) permits the hypothesis that CE and BuCE play a more significant role as "points of loss" in development of the toxic effect of the phosphates in question, in comparison with methylphosphonates. The significant decrease in the toxic effect of dialkylthiophosphates IX with growth of hydrophobicity, which correlates with growth of the affinity of IX to enzymes serving as "points of loss", is also an

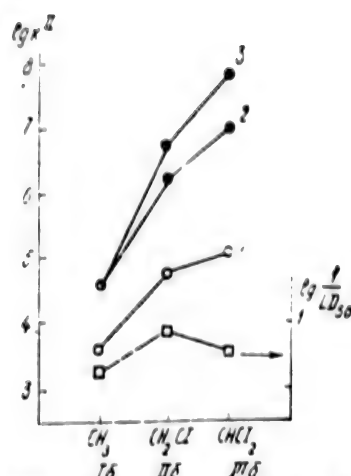
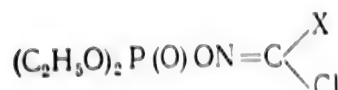


Figure 3. Dependence of Antienzymatic Activity and Toxicity of Diethylphosphates $(C_2H_5O)_2P(O)ON=C^X$ on the Number of Chlorine Atoms in the Outgoing Group: 1—ACE; 2—BuCE; 3—CE

indication of the significant role played by CE and BuCE in development of the toxic effect of phosphates (Figure 2b).

As was shown above, antiesterase activity of phosphorylated alkyl-chloroformoximes grows with increasing number of chlorine atoms in the outgoing group; however, correlation is not observed between growth of

anti-ACE activity and change in toxicity. Figure 3 shows the dependence of the constants of inhibition of ACE, BuCE and CE and the toxicity of diethylphosphates on



the number of chlorine atoms in the outgoing group ($X = CH_3$ - Ib; CH_2Cl - IIb; $CHCl_2$ - IIIb). Compound IIIb inhibits CE and BuCE correspondingly 14 and 6 times more effectively than IIb; in this case, they differ in their anti-ACE activity by only two times, which made it possible to hypothesize elevated expenditure of compounds IIIb at the "loss points", CE and BuCE, in the whole organism, leading to a lower effective concentration of this compound at the biotarget. To verify this hypothesis we studied the antienzymatic activity of compounds IIb and IIIb in experiments on whole animals (mice) receiving systemic doses. It was established that one-time administration of IIb and IIIb in doses equivalent to $0.15 LD_{50}$ leads to fast and significant inhibition of blood cholinesterases (Figure 4). When the dose is increased to $0.3 LD_{50}$, we observe clearly pronounced inhibition of both blood and liver esterases (Figure 5). In all cases compound IIIb inhibits Ce and BuCE more intensively than IIb. The activity of brain ACE in response to administration of these compounds in the investigated doses did not change. These data show that binding with CE and BuCE—esterases serving as "loss points"—makes a significant contribution to the development of the toxic effect of the phosphorylated

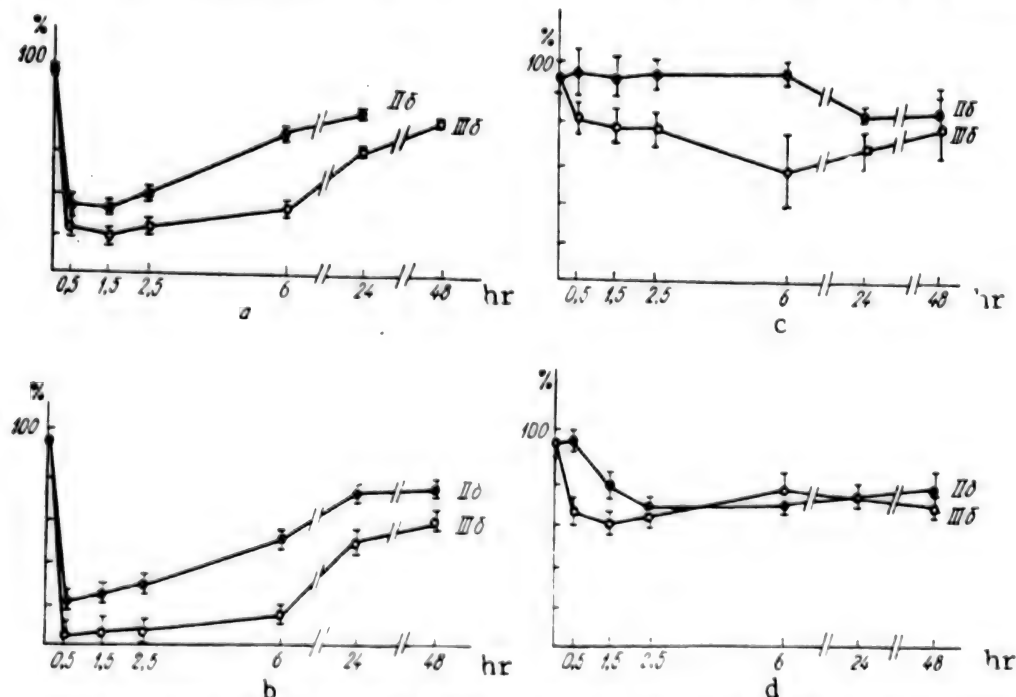


Figure 4. Dynamics of Change in Blood and Liver Esterase Activity in Response to Systemic Administration of Compounds IIb and IIIb at a Dose of $0.15 LD_{50}$: a—whole blood CE; b—plasma CE; c—liver CE; d—liver CE (percent of control)

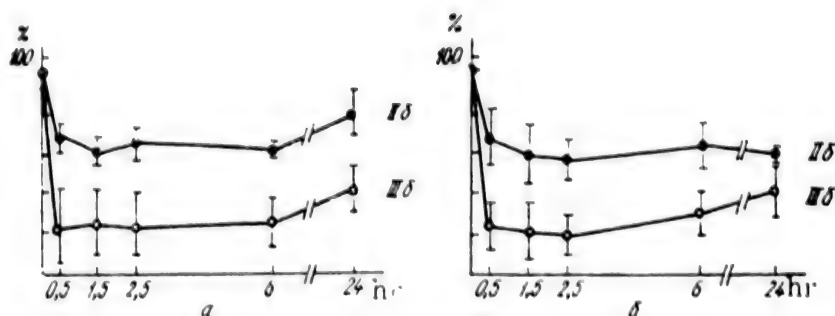


Figure 5. Dynamics of Change in Liver Esterase Activity in Response to Systemic Administration of Compounds IIb and IIIb at a Dose of 0.3 LD₅₀: a—liver CE; b—liver CE (percent of control)

alkyl-chloroformoximes in question. In this case, when doses are small, blood esterases play the predominant role as "loss points", while when the dose is increased, significant loss of the substance occurs due to binding with liver CE and BuCE. The fact that the toxicity of IIIb is lower than expected is explained both by its lower hydrolytic stability ($K^1 = 0.27 \text{ min}^{-1}$; pH 9.0; 25°C) and by predominant growth of affinity to enzymes serving as "loss points"—CE and BuCE—upon introduction of a second chlorine atom.

Thus, the research reveals that CE and BuCE play a significant role in development of the toxic effect of organo-phosphoric pesticides. Systematic research on the antiesterase properties of organo-phosphoric pesticides in experiments and *in vitro* on whole animals, including determination of anti-BuCE and anti-CE activity in addition to evaluation of anti-ACE activity, makes it possible to characterize more fully the biochemical factors which make a contribution to the toxicity of organo-phosphoric pesticides, and to predict it with greater justification.

Description of Experiments

Commercial, domestically produced ACE and BuCE preparations, corresponding with relative activity of 4 and 9.6 units/mg protein, and pig liver CE preparation with relative activity of 100 units/mg protein (Sigma, USA), were used. Kinetic measurements were made potentiometrically under constant pH conditions in an RTS-822 autotitrator (Radiometer, Denmark) under standard conditions (25°C; 0.1 M KCl; 1.33 mM phosphate buffer, pH 7.5 for cholinesterases using acetylcholine as the substrate, and pH 7.8 for CE using ethylbutyrate as the substrate). The bimolecular rate constants for interaction of esterases with inhibitors (k^1) were determined as in [14] under the conditions $[I]_0 \gg [E]_0$, monitoring the residual activity of the enzyme following incubation with the inhibitor. The constants were calculated by linear regression using an HP-67 computer (USA). Acute toxicity was determined in experiments on white mongrel mice weighing 18 - 24 gm. All substances were dissolved in aqueous acetone solution and injected

intraperitoneally. The LD₅₀ was determined by calculation using a NORD-10 computer (Norway) by the method described in [15]. Cholinesterase activity in animal (mouse) tissues was determined in different time intervals after one-time administration of the substances (intraperitoneally) by Ellman's method using a Gilford spectrophotometer (USA) at $\lambda = 412 \text{ nm}$; acetyl- and butyrylthiocholine were used as substrates. Carboxylesterase activity was determined potentiometrically under constant pH conditions with a pH-262 pH-meter, and ethylbutyrate as the substrate.

Bibliography

1. Melnikov, N. N., "Pestitsidy. Khimiya, tekhnologiya i primeneniye" [Pesticides. Chemistry, Technology, Use], Moscow, Khimiya, 1987, p 712.
2. Golikov, S. N., Sanotskiy, I. V. and Tiunov, L. A., "Obshchiye mekhanizmy toksicheskogo deystviya" [General Mechanisms of Toxic Action], Leningrad, Meditsina, 1986, p 280.
3. Kagan, Yu. S., "Toksikologiya fosfororganicheskikh pestitsidov" [Toxicology of Organophosphoric Pesticides], Moscow, Meditsina, 1977, p 298.
4. Rozengart, V. I. and Sherstobitov, O. Ye., "Izбирatel'naya toksichnost fosfororganicheskikh insektoakaritsidov" [Selective Toxicity of Organophosphoric Insectoacaricides], Leningrad, Nauka, 1978, p 173.
5. Murphy, S. D., Cheever, K. L., Chow, A. Y. K. and Brewster, M., "Organophosphate Insecticide Potentiation by Carboxylesterase Inhibitors," PROC. EUR. SOC. TOXICOL., Vol 17, 1976, pp 292-300.
6. Boskovic, B., "The Influence of 2-(O-Cresyl)-4H-1,3,2-Benzodioxaphosphorin-2-Oxide (CBDP) on Organophosphate Poisoning and Its Treatment," ARCH. TOXICOL., Vol 42, 1979, pp 207-216.
7. Martynov, I. V., Ivanov, A. N., Yepishina, T. A. et al., "Interaction of Polychloronitrosoethanes With Phosphorous Acid Derivatives," IZV. AN SSSR. SER. KHIM., No 5, pp 1086-1089.

8. Ivanov, A. N., Yepishina, T. A., Goreva, T. V. et al., "Interaction of Dialkylphosphites With 1,1-Dichloronitrosoalkanes," *IZV. AN SSSR. SER. KHIM.*, No 1, 1987, pp 226-228.

9. Eto, M., "Organophosphorus Pesticides," Boca Raton: GRC, 1979, p 387.

10. Makhayeva, G. F., Shatayeva, G. A., Yankovskaya, V. L. et al., "Interaction of Bis-Phosphorylated Methanes With Mammalian Esterases," *BIOORGAN. KHIMIYA*, Vol 10 No 10, 1984, pp 1347-1352.

11. Fetisov, V. I., Mikhayeva, G. F., Loshadkin, N. A. et al., "Nonlinear 'Hydrophoby-Antiesterase Activity' Model for Some Types of Organophosphoric Compounds," *BIOORGAN. KHIMIYA*, Vol 10 No 10, 1984, pp 1353-1358.

12. Makhayeva, G. F., Fetisov, V. I., Sokolov, V. B. et al., "Interaction of Dialkyl (α -Karbomethoxy- β , β -Trifluoroethyl) Phosphates With Mammalian Esterases," *BIOORGAN. KHIMIYA*, Vol 13 No 1, 1987, pp 33-37.

13. Hansch, C. and Leo, A., "Substituent Constants for Correlation Analysis in Chemistry and Biology," New York: Wiley, 1979, p 339.

14. Yakovlev, V. A., "Kinetika fermentativnogo kataliza" [Kinetics of Enzymatic Catalysis], Moscow, Nauka, 1965, p 248.

15. Litchfield, J. T. and Wilcoxon, F., "A Simplified Method of Evaluating Dose-Effect Experiments," *J. PHARM. EXP. THERAP.*, Vol 96 No 2, 1949, pp 699-113.

Article Synopses

Romanov, N. N. and Fedotov, K. V., "Thiazolo[3,2-a]Pyrimidines. Synthesis and Physiological Activity (A Survey)...", pp 1-12. UDC 547.789.26118

Published data on the synthesis, chemical properties and physiological activity of compounds of the thiazolo[3,2-a]pyrimidine series are surveyed. 165 bibliographic references.

Shevchenko, L. I., Kutsenko, T. A., Lozinskiy, M. O., Tatarova, T. A. and Skoroded, T. M., "Study of the Dependence of Physiological Activity on Structure of Derivatives of *p*-Aminomethylbenzoic Acid", pp 18-20. UDC 547.466+581:541.123:615.281

The anti-fibrinolytic, anti-inflammatory and anti-microbial action of N-substituted derivatives of *p*-aminomethylbenzoic acid at the amino and carboxyl group is studied. It is demonstrated that substitution of hydrogen atoms in the amino group of *p*-aminomethylbenzoic acid reduces its anti-fibrinolytic activity. Some derivatives at the carboxyl group that

retain high anti-fibrinolytic activity also exhibit significant anti-inflammatory and anti-microbial action. 2 tables; 10 bibliographic references

Golovenko, N. Ya., Zinkovskiy, V. G., Rydenko, O. P., Totrova, M. Yu. and Povolotskaya, O. P., "Anxiolytic and Soporific Action of Peptidamidobenzophenones", pp 20-25. UDC 615.213:547.964.4].07

The anti-aggressive and myorelaxant action, effect on exploratory behavior and motor activity and potentiation of the effects of barbiturates of a number of derivatives of 5-bromo-2-peptidamidobenzophenone depending on time and means of their administration to mice are subjected to comparative analysis. Significant differences in pharmacological activity that depend on the structure of the hetero-fragment of the PABP molecule are established. The length of time the physiological action of PABP's manifests itself was determined by the means of their administration

Multifactorial dispersion analysis of the dynamics of the anticonvulsive effect recorded after administration of the compounds made it possible to quantitatively assess the influence of modifications of their structure on physiological activity. The most significant increase in pharmacological activity of PABP's was observed after methylation of the compound's 2-amide radical. Modifications of the structure of the peptide fragment of the PABP molecule led to significant but less pronounced changes in the anticonvulsive activity of the compounds. 1 figure; 6 tables; 7 bibliographic references.

Khaskin, I. G. (deceased), Korshun, M. N., Dyachina, Zh. S. and Begunov, G. A., "Relationship of the Structure, Acute Toxicity and Susceptibility to Biological Breakdown of Some Diarylmethanes", pp 25-30. UDC 547.631.2:615.9:543.39

The acute toxicity and susceptibility to biological breakdown of diphenylmethane, some of its homologues, chlorine and alkoxy-derivatives are determined. Qualitative dependencies of these properties on steric factors and electron shifts elicited by substituents are found. 3 tables; 3 bibliographic references.

Barilyak, I. R., "Relationship Between Chemical Structure and Embryotoxicity of Glycols", pp 30-33. UDC 613.632-07

The effect of mono-, di-, tri-, tetra- and pentaethyleneglycols (with intragastric administration) and of diethyleneglycol, ethylglycolacetate, and the methyl and butyl ethers of ethyleneglycol (with inhalational administration) upon intrauterine development is studied in experiments on white rats. It is demonstrated that glycols and their ethers are lethal to embryos and teratogenic owing to features of the chemical structure of the substance. 1 figure; 2 tables; 10 bibliographic references.

Korchak, V. I., Samoylov, A. P., Karachunova, S. I. and Gupalo, Yu. M., "Effect of Chloro-Derivatives of *p*-Tert-Butyltoluene (PTBT) on the Liver", pp 33-36. UDC 547.53.211 2:577.15.085

The effect of different concentrations of chlorinated *p*-tert-butyltoluenes on the activity of alaninaminotransferase in blood serum and the morphological state of the liver from 1, 24 and 72 hours after 4 hours of inhalation of *p*-tert-butyltoluene and mono-, di- and trichloro-*p*-tert-butyltoluene were studied in acute experiments on rats. It was established that as the degree of chlorination of *p*-tert-butyltoluene increases, the reaction of liver parenchyma to it decreases. 1 table; 6 bibliographic references.

Sinitskaya, T. A. and Bakhishev, G. N., "Interaction of 3-Oxy-5- Methyloxazole With Artificial Phospholipid Membranes", pp 36-39. UDC 615.9+577.3

Interaction of butsid with model hydrophobic systems possessing two macroscopic water-lipid interfaces (flat artificial phospholipid membranes) and with one interface (an interface between water and a solution of azolektin [transliteration] in decane) is studied in an experiment. It is established that butsid is capable of interacting with the lipid phase of biomembranes, and thus having an influence both on the properties of the membranes themselves and on membrane-bound systems; it has a limited capability for penetrating through artificial phospholipid membranes with the concentration gradient, and for accumulating in the lipid phase of artificial phospholipid membranes. It can act upon biomembranes in similar fashion as well. 2 figures; 16 bibliographic references.

Petrenko, V. S., Borisevich, A. N., Stepura, G. S., Mozgovaya, G. P., Samoylenko, L. S. and Rodinov, A. P., "Synthesis and Growth Regulating Properties of Acyl-Substituted Thiophene and Thiolene", pp 39-44.

The reaction of arylamides of α -phenylaminomethylidene- β -ketothionbutyric acid with α -halocarbonyl compounds was used to obtain acyl-substituted thiophene and thiolene, and their growth regulating properties in relation to some mono- and dicotyledon plants, auxin activity and phytotoxicity were studied. Thiophene derivatives, among which both plant growth inhibitors and stimulators were revealed, were found to be the most active compounds. 2 tables; 13 bibliographic references.

Bezuglyy, Yu. V., Boreyko, V. K., Bylina, Ye. V., Tukhar, A. A., Foremnaya, V. P. and Khilchuk, S. P., "Synthesis and Growth Regulating Activity of Sulfur-Containing Derivatives of Five-Membered Cyclic Sulfones", pp 44-49. UDC 631.811.98

The growth regulating action of sulfur-containing derivatives of thiolane- and thiolene-1,1-dioxides on test objects was studied. Some compounds were established to have high inhibitory activity in relation to wheat sprouts, exceeding that of the standard preparation—maleic acid hydrazide. A certain dependence of the

activity of the substances on their structure was revealed. 1 table; 11 bibliographic references.

Reydalova, L. I., Borisenko, V. P., Maydanovich, N. K., Sinitsa, A. D. and Stepura, G. S., "Growth Regulating Activity of N-Alkyl-N-2,2-Dimethylvinylamidophosphates", pp 49-52. UDC 547.583.5+541.69+632.934

It is demonstrated that growth regulating activity decreases in the transition from butadienylamidophosphates to vinylphosphonates isomeric with them, and that it depends on the nature of the substituents at the nitrogen and phosphorus atoms. 2 tables; 12 bibliographic references.

Belenkaya, I. A., Prokhorechuk, Ye. A., Uskova, L. A., Shulla, T. A., Sirik, S. A., Goritskaya, E. F. and Grib, O. K., "Study of the Insectoacaricidal Activity of Nitro-Derivatives of Benzo-2,1,3-Thia- and Selenadiazoles", pp 52-56. UDC 547.794.3

The insectoacaricidal activity of nitro-derivatives of benzo-2,1,3-thia- and selenadiazoles is studied. The program for statistical treatment of the results using an Elektronika BK 0010 microcomputer is presented. 4-Nitrobenzo-2,1,3-selenadiazole and 4-oxy-5-nitrobenzo-2,1,3-thiadiazole were discovered to have high selective insecticidal activity. The LD₅₀ of these compounds was determined. Acquisition of some nitro-derivatives and an intermediate product—4-chloro-5-methylbenzo-2,1,3-thiadiazole—is described. 1 table; 21 bibliographic references.

Belenkaya, I. A., Dyachina, Zh. S., Shulla, T. A., Prokhorechuk, Ye. A., Uskova, L. A. and Grib, O. K., "Study of the Fungibactericidal, Insecticidal and Nematocidal Action of Complex Compounds Consisting of Bivalent Cobalt and Copper and Oxy- and Mercapto-benzo-2,1,3-Thiadiazoles", pp 56-60. UDC 547.794.3

The fungibactericidal, insectoacaricidal and nematocidal activity of bivalent cobalt and copper complexes of oxy- and mercapto-benzo-2,1,3-thiadiazoles is studied. Complex compounds based on 4-oxy-, 4-oxy-5-nitro- and 4-mercaptobenzo-2,1,3-thiadiazoles were discovered to have high insecticidal and (or) fungicidal activity. It is demonstrated that the effectiveness of complex compounds and ligands is not consistent in relation to test objects, and that copper complexes based on the same ligand are more effective than cobalt complexes. Methods of obtaining complex compounds and mercaptans in the benzo-2,1,3-thiadiazole series are described. 3 tables; 8 bibliographic references.

Kostina, V. G., Rutkovskiy, E. K., Musich, Ye. G., Feshchenko, N. G. and Petrenko, V. S., "Synthesis and Fungicidal Properties of Tetrakis (Aryl- and Arylalkylamido) Phosphonium Salts", pp 60-64. UDC 547.241+632.952

Synthesis of tetrakis(arylamido)phosphonium iodides, triiodides, carbacyls and sulfonates, as well as of tetrakis(arylalkylamido)phosphonium iodides is described.

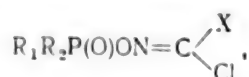
The fungicidal activity of the obtained compounds on pure cultures of phytopathogenic fungi is studied. It is demonstrated that tetrakis(arylamido)phosphonium triiodides and tetrakis(arylalkylamido)phosphonium iodides are the most active, with the fungicidal activity of the latter growing as the length of the alkyl radical decreases, but in this case acute toxicity in relation to homeotherms rises as well. 2 tables; 4 bibliographic references.

Merezhinskiy, Yu. G., Shvartau, V. V., Fedorenko, Yu. P., Tochilkina, L. M. and Kudrya, T. N., "Herbicidal Activity of Dibenzo-18-Crown-6 and Its Derivatives", pp 64-68. UDC 632.954.547.26.118

It is established that dibenzo-18-6 and its derivatives possess potential phytotoxicity at the level of the photosynthetic system of plants in addition to low phytotoxicity in relation to the sprouts of mono- and dicotyledons, and that they effectively raise the activity of known herbicides. 3 tables; 9 bibliographic references.

Makhayeva, G. F., Yankovskaya, V. L., Kochetova, L. M., Beznosko, B. K., Sokolov, V. B., Brel, V. K., Malygin, V. V. and Martynov, I. V., "Investigation of the Interaction of O-Phosphorylated Oximes With Homeotherm Esterases. The Role of Esterases in Toxicity", pp 68-74. UDC 547.26 118:577.152.311.042:541.697 +519.237.5

Investigating the biochemical mechanisms responsible for development of the toxicity of O-phosphorylated oximes with the general formula where $R_1 = R_2 = \text{AlkO}$,



$R_1 = \text{CH}_3$, $R_2 = \text{AlkO}$, $R_1 = R_2 = \text{AlkS}$, $X = \text{Alk}$, CH_2Cl , CHCl_2 , synthesized as potential pesticides, was the goal of studying the kinetics of their interaction with the esterases of homeotherms and determining their acute toxicity. It was established that hydrophobic interactions are the determining factor in inhibition of carboxylesterase and butyrylcholinesterase—enzymes serving as "points of loss" of organophosphoric compounds in the organism—by these compounds. The significant role played by the alkylchloroformoxime group in sorption of phosphates in the active center of acetylcholinesterase is demonstrated. Experiments *in vitro* and on whole animals established that phosphorylation of nonspecific esterases, CE and BuCE, makes a significant contribution to development of the toxicity of the investigated compounds. 5 figures; 1 table; 15 bibliographic references.

Khaytin, M. I., Simkina, Yu. N., Sukhov, A. G. and Stradomskiy, Yu. V., "Psychopharmacological Study of Competitive Relationships Between Uridine and Thymidine," pp 74-76. UDC 615.214.22

It was established in experiments on tetrahybrid CBA mice that the pyrimidine nucleoside thymidine produces

characteristic behavioral signs of anxiety at a dose of 25 mg/kg 60 min after intraperitoneal administration (conflict-type actions, reduction of the number of movements between the dark and light compartments of a shuttle chamber), which combine with indicators of a depression-like state (an increase in immobilization time in the "behavioral despair" test, suppression of active forms of intraspecific communicativeness). The pyrimidine nucleoside uridine, which possesses anxiolytic and antidepressant action at a dose of 12.5 mg/kg, significantly weakened or completely neutralized the behavioral disorders elicited by thymidine at lower doses (3.125 and 6.25 mg/kg). The results permit the hypothesis that competitive relationships exist between uridine and thymidine, and that an elevated concentration in the organism raises the effectiveness with which brain structures react to uridine. 2 tables; 10 bibliographic references.

Yutilov, Yu. M., Ignatenko, A. G., Andreyeva, Ye. I., Bobkova, G. V. and Mikhaylova, L. Ye., "Synthesis and Fungicidal Activity of Styryl Derivatives of Imidazo(4,5-c)Pyridine", pp 77-80. UDC 547.785.5 821:632.952

Styryl derivatives of quaternary salts of imidazo(4,5-c)pyridine were synthesized and the fungicidal activity of the resulting compounds was investigated against fungal mycelia and on green plants against downy mildew of cucumbers as well as late blight of tomato. Compounds containing *p*-dimethylamino- and 2,5-dimethoxystyryl substituents in the pyridine fragment of the molecule possessed the highest fungicidal activity. The structure of the obtained styryl derivatives of imidazo(4,5-c)pyridine was demonstrated with data from PMR spectroscopy using compounds containing a trideuteromethyl group in position 4 on the pyridine ring.

Duzhak, V. G., "Chemical Structure and Antiadrenergic Properties of Hydrogen Halide Salts of Aralkylisothiuronium," pp 81-83. UDC 615.015.11:615.214.24:615.217.5:615.225.2

The relationship between the chemical structure of halide hydrates of aralkylisothiuronium and their physiological effects is studied. Introduction of a chlorine atom or a nitro group in different positions on the aromatic ring changes the properties of aralkylisothiuronium salts in the direction of predominant action upon presynaptic adrenergic processes. Alkylation of the two nitrogen atoms of the amidine grouping by methyl groups sharply increases the substance's toxicity and results in loss of α_1 -adrenolytic action. This effect is also noted in the *m*-chloro-substituted salt. 1 table, 14 bibliographic references.

Mirskova, A. N., Drozdova, I. T., Levkovskaya, G. G., Gogoberidze, I. T., Ochirov, Yu. D., Zarubina, V. N., Zhovtiy, I. F. and Voronkov, M. G., "Synthesis of

N-(1-R-2,2-Dichloroethyl) and N-(1-R-2,2,2-Trichloroethyl) Arylsulfonylamides and Their Activity in Relation to Disease Vectors—The Fleas *Xenopsylla cheopis* and *Ceratophylles anisus*", pp 84-89. UDC 615.212/213:544.352.012

New N-(1-R-2,2-dichloroethyl)- and N-(1-R-2,2,2-trichloroethyl) arylsulfonylamides— $\text{CCl}_2\text{VCH(R)NHSO}_2\text{Ar}$ —were synthesized. Their activity was studied in relation to vectors of infectious diseases—the fleas *Xenopsylla cheopis* and *Ceratophylles anisus*. It was established that most polychlorinated arylsulfonylamides have clearly pronounced insecticidal activity. 2 tables; 10 bibliographic references.

Kuryata, V. G. and Dabizhuk, T. M., "Action of Retardants on Morphogenesis and Productivity of Raspberry Runners", pp 89-92. UDC 631.811.98:634.711

The activity of chlorocholine chloride and a number of ethylene producers in relation to raspberry plantations was subjected to comparative study. It was revealed that use of retardants is an effective means of chemical

regulation of the morphogenesis and production of raspberry plantations, with treatment by ethylene producers being preferable owing to milder action upon the plant than chlorocholine chloride. 2 figures; 1 table; 13 bibliographic references.

Kolesnik, Yu. R., Grib, O. K., Uskova, L. A. and Svetkin, Yu. V., "Growth Regulating Activity of Pesticides Immobilized on Poly-2-Methyl-5-Vinyl-1-Pyridiniummethylenepentamethyldisiloxane", pp 92-96. UDC 546.87+631.811

Known herbicides and plant growth regulators were immobilized on a polymer organosilicon water-soluble carrier, and the inhibitory and stimulatory effects of polymer forms on plants were studied.

It was established that polymer complexes of pikloram and 2,4-D are inferior in activity to monomer forms. The herbicidal effect sets in after a long exposure time, and it manifests itself as death and formative changes in plants, followed by their withering. The polymer complex of naphthylacetic acid possesses auxin-like action superior to the standard. Polygibberellinate possesses growth regulating action inferior to that of gibberellic acid.

Health Care System and AIDS

917C00124 Moscow VETERAN in Russian No 32,
6-12 Aug 90 p 15

[Article by T. Bystrova: "Hostages"]

[Excerpt] Wouldn't it be interesting if, in announcing his program, Academician Chasov had foreseen that here, in contrast to civilized countries throughout the world, where the main sources of the infection are drug addicts, homosexuals and prostitutes, medical institutions have become its breeding grounds? If anyone he, as minister, would have at his disposal the information about the equipment at his clinics, hospitals and aid stations, about the training of his specialists, and generally, about what is being done in our health care system.

Nevertheless, AIDS took us by surprise. We were not prepared for our "encounter" with it. Its first victim died more than a year ago. AIDS has now claimed 19 lives, while more than 500 people have been diagnosed as carriers of the virus. The majority of them are children. Infected individuals have been found in 11 republics. The total is about 1,000. Scientists predict that the number of infected individuals will steadily increase, reaching 89,000 by 1993 and, 50 million by 2006. Of course, such predictions cannot be absolutely correct. Firstly, they are oriented towards the present standards of Soviet health care. Secondly, it is not known how the virus will behave in the future, how people's behavior will change as a result of danger, and what medicines scientists will develop.

There are now no effective methods for fighting AIDS. Two preparations have some effect upon the HIV: Azidothymidine and ribovirin. They only temporarily suppress the reproduction of the virus. Recently, the English announced the invention of yet another drug, "dideoxynosine", and Austrian specialists are testing a new vaccine—glycoprotein-160. Among the medicines known to prolong the life of those with the virus are interleukin-2, T-activine, and interferon, all of which have a stimulating effect upon the immune system.

There are interesting developments by the Moscow and Novosibirsk scientists D. Knoppe, N. Grinevaya, R. Salganik and Z. Shabarovaya. They have developed chemical compounds that penetrate cells, bond to them at a specific site on a nucleic acid molecule (these are basic to the virus) and change its structure. This always disables the virus. It is to be hoped that this discovery will be nominated for a Lenin Prize and not remain a laboratory curiosity, but start being generally introduced in medical practice.

So, at present, not a single citizen in our country is safe from the threat of AIDS. This was stressed at a meeting of the interagency council for propaganda on AIDS prevention. Incredible facts were presented here.

—There is a catastrophic shortage of disposable syringes. Last year the USSR Ministry of Health obtained 500

million; this year it will obtain 650 million. The country's total annual requirements are 6 billion.

—Medical institutions have only one-third of the sterilizers they need.

—There are no disposable stomatological probes.

—Gynecologists do not have enough protective gloves.

—One cannot buy condoms at drugstores.

—There are not enough endoscopes for examining people with gastrointestinal disorders. As a rule, 7 - 10 examinations per day are made with 1 - 2 endoscopes that have not been sufficiently sterilized. Methodological instructions for disinfection are only being prepared for publication.

—The demand for blood substitutes is only being half met. Because they fear getting AIDS, donors are refusing to give blood and patients are refusing to accept it.

—There are not enough test systems for diagnosing AIDS or HIV infection. Thus, it is quite probable that thousands of unaware carriers of the virus are among us. Many of the 812 diagnostic laboratories in the country have to work without this equipment.

So, none of us can have any peace of mind after visiting an outpatient clinic. We cannot be sure whether, after getting rid of one ailment, we will not have been infected with one even more dangerous.

All of us, old and young, are hostages to our health care system and medical industry.

This year the USSR Supreme Soviet passed a decree, "On the Prevention of AIDS", that makes provisions for increasing the responsibility of medical workers, assuring the protection of the rights of those infected and protecting the public from the spread of AIDS. Even though it is clear that no document can save us from infection, this was a necessary step in the struggle against AIDS. The lives of millions of Soviet people are involved.

So that nobody will think that these are simply words, it is appropriate to conclude with another forecast by scientists. As you well know, these are not made by reading tea leaves, but with the help of modern scientific methods: There is a threat that in the first decade of the next century up to 40 percent of the younger generation in our country will die of AIDS. This is not far off.

Ministry of Health Scientific Center Explains Chernovtsy Illness

917C00144 Moscow SEMYA in Russian No 32,
6-12 Aug 90 p 11

[Article by V. Popkov: "Who Is Guilty? A New Investigation Attempt"]

[Abstract] Following repeated unsuccessful attempts to isolate the cause of the Chernovtsy illness, a group of specialists from the Scientific Center of Molecular Diagnostics, USSR Ministry of Health, investigated this problem. An increase in upper respiratory infections, asthma attacks, exacerbation of liver pain, and hair loss, predominantly in children, had been associated with the Chernovtsy illness. Thallium in the coal used to heat homes causes hair loss, so afflicted families sought another means of heating their homes, with factories providing a ready solution—their recycled waste, which factory administrators knew to be toxic. Ironically, the source of the problem was linked to environmental cleanup efforts by administrators in factories that produced clay-like slurry containing borates, fluorides, heavy metals, and other toxic substances. These wastes were used as raw materials in the production of construction materials with the administrators' full knowledge that the heating of these toxic wastes would release pollutants—borofluoride, compounds whose salts with heavy metals and sodium were very water-soluble. Problems hindering earlier investigations included a desire to blame illnesses on a source outside the city, such as imported raisins and nuts, acid rain, etc., and failure to give the complete details of the illnesses to World Health Organization investigators.

Difficulties in Diagnosing AIDS in Uzbekistan

917C0016A Tashkent KOMSOMOLETS
UZBEKISTAN 20 Jul 90 p 4

[Article by Ye. Lamikhova: "Doomed as Number Five"]

[Abstract] This follow-up article to a previous news story about a nurse who contracted the AIDS virus while performing a blood transfusion revealed new information on the AIDS situation in Uzbekistan. While the Tashkent Municipal AIDS Control Center refused to give any information, other sources revealed that there were about 100 false positive cases of AIDS in the republic. In this situation, people classified as false positive cases were those who experienced AIDS-like symptoms, but analyses did not support an AIDS diagnosis. The problem is that not one of the 13 AIDS control centers, the hundreds of laboratories that test for the human immunodeficiency virus, or the anonymous testing clinics throughout Uzbekistan has the test that can yield conclusive results. The first test can only indicate a serious disorder, while the second, conclusive test can only be performed in Moscow at considerable expense. If the rumor now circulating in medical circles of yet another AIDS virus carrier were true, it would be the 16th case in Uzbekistan in recent years, the fifth among Soviet citizens.

Special Scientific Session on Perinatal Pathology and Infant Mortality Held in Tashkent

917C00851 Moscow VESTNIK AKADEMII
MEDITSINSKIKH NAUK SSSR in Russian No. 7,
Jul 90 pp 3-4

[Article: "Out-of-Town Joint Scientific Session of the Department of Clinical Medicine and the Department of

Hygiene, Microbiology and Epidemiology of the USSR Academy of Medical Sciences, the USSR Ministry of Health, the Uzbek SSR Ministry of Health, the Uzbek SSR Academy of Sciences, the USSR Academy of Medical Sciences Scientific Research Institute of Pediatrics, the USSR Ministry of Health All-Union Scientific Research Center for Protection of the Health of the Mother and Child, the Uzbek SSR Ministry of Health Scientific Research Institute of Pediatrics, the All-Union Scientific Society of Pediatricians and the All-Union Scientific Society of Obstetrician-Gynecologists on the Problem 'Perinatal Pathology and Infant Mortality,' Tashkent, 17-19 October 1989"; the proceedings are published in No 7 and No 8, 1990]

[Text] Five hundred ninety representatives of medical science and Soviet public health took part in the work of the session, including six academicians of the AMN SSSR [USSR Academy of Medical Sciences], nine corresponding members of the AMN SSSR, one academician of the Uzbek SSR Academy of Sciences, one corresponding member of the Uzbek SSR Academy of Sciences, 38 professors, 11 doctors of sciences, 125 candidates of medical sciences and 122 physicians (from practical public health institutions of the Uzbek SSR) from nine unions (RSFSR, Uzbek SSR, Ukrainian SSR, Belorussian SSR, Lithuanian SSR, Tajik SSR, Kirghiz SSR, Turkmen SSR, Kazakh SSR) and two autonomous republics (Dagestan and Kara-Kalpak) and 19 cities.

Uzbek SSR Minister of Health M. Bakhramov and USSR Ministry of Health deputy chief of the main administration of protection of maternity and childhood, I. A. Leshkevich, took part in the session's work.

Twenty-four reports were given at the session. Four of the speakers presented materials from research conducted in Uzbekistan. Ten persons participated in the discussion.

The reports and statements illuminated regional problems of perinatal pathology and infant mortality, proposed a program for reducing infant mortality in the Uzbek SSR, described the organization of medical care for women and children under the conditions of the new economic mechanism, illuminated the influence of ecological factors on the course of gestation, demonstrated the influence of genetic factors on perinatal mortality, and reflected other aspects of the problem of "Perinatal Pathology and Infant Mortality."

It was emphasized at the session that there was great significance to conducting it in the country's Central Asian region, where perinatal and infant mortality is so high. The dynamics and trends in perinatal and infant mortality in the USSR and in the Uzbek SSR were analyzed in the reports. Some positive changes in this pathology were noted, although child mortality continues to be very high.

The most important causes of mortality in different regions were clarified. In particular, causes in the Uzbek

SSR include the influence of the environment, traditions, insufficient protein nutrition and vitamin imbalance. Certain shortcomings exist in the organization of medical care. Materials pertaining to the dynamics and etiological factors of the development of pneumonia in children up to one year of life are very important. It was shown that *Klebsiella* and *Chlamydia*, which are hard to fight by traditional methods, are acquiring increasingly greater significance. The need for centralized payment of the costs of interferon treatment of children in their first week of life was substantiated.

Materials that may help public health organs increase their efforts against children's infections were presented in many reports.

The session resolved to ask the Presidium of the AMN SSSR to do the following:

1. To petition the USSR State Committee for Science and Technology to include the problem of "Protection of the Health of the Mother and Child" among the priority scientific and technical programs, and to support its fulfillment with the necessary materials, equipment and financing from the state budget.
2. To examine the issue of including expert councils of a clinical direction within the composition of the scientific councils of the AMN SSSR, and to define their functions more clearly. To resolve the issue of supplementary financing of priority scientific research.
3. To examine the issue of the suitability of transferring, to the AMN SSSR, the USSR Ministry of Health's All-Union Scientific Research Center for the Protection of the Health of the Mother and Child—the country's head institution on the problem of obstetrics and gynecology.
4. To petition the USSR Ministry of Health to increase yearly allocations to the financing of scientific research on pediatrics, obstetrics and gynecology; to finance republic scientific programs in accordance with the grant provided to republic centers for the protection of the health of the mother and child; to support introduction of the principal scientific accomplishments into practical public health, and to ensure that the chief specialists of the USSR Ministry of Health, the union republic ministries of health, and of the krais, oblasts and cities maintain systematic control over this; to initiate, as quickly as possible, production of mother's milk substitutes, food products for children of nursing age, specialized products for the nutrition of premature infants, and therapeutic products for children with hereditary diseases, food allergies and the impaired absorption syndrome, with regard for regional features (jointly with the All-Union Detskoye Pitaniye Scientific-Production Association); to intensify epidemiological surveillance at maternity hospitals, and to examine the issue of creating a service to study bacterial flora in therapeutic-preventive, obstetric and children's institutions.

In addition, it was recognized as necessary:

- for scientific councils of the AMN SSSR on obstetrics and gynecology, pediatrics, hygiene, microbiology and medical problems of nutrition to increase the volume of fundamental scientific research with the purpose of studying different problems of perinatal pathology more deeply;
- for the AMN SSSR scientific council on obstetrics and gynecology and the AMN SSSR scientific council on pediatrics to expand research on the scientific directions of the greatest priority: study of adaptation of the mother, the fetus and the infant to ecological, including chemical, factors; research on miscarriages; development of the methods of early diagnosis and treatment of the respiratory distress syndrome, caring for premature infants with central nervous system damage, and their early rehabilitation; research on the influence of a complicated pregnancy and delivery on the state of the fetus and infant; research on the problems of intrauterine infection and AIDS;
- for the AMN SSSR scientific council on hygiene to expand research on the influence of chemical contamination of the environment upon the health of children;
- for the AMN SSSR scientific council on medical problems of nutrition, the AMN SSSR scientific council on obstetrics and gynecology and the AMN SSSR scientific council on pediatrics to foresee, in their scientific research plan for 1990-1995, research aimed at developing physiological norms for the nutrient demands of pregnant and nursing women as well as of infants and young children, with the purpose of establishing a sensible diet for them and reducing morbidity and child mortality.

COPYRIGHT: Izdatelstvo "Meditsina", 1990

Regional Features of Infant Mortality

917C0085B Moscow VESTNIK AKADEMII
MEDITSINSKIKH NAUK SSSR in Russian No 7,
Jul 90 pp 6-9

[Article by M. Ya. Studenikin, Ye. A. Leparskiy and N. P. Makelskaya. USSR Academy of Medical Sciences Scientific Research Institute of Pediatrics, Moscow]

UDC 616-053.31:312.2]-07(47+57)

[Text] The "Basic Directions for the Development of Protection of Public Health and Restructuring of USSR Public Health in the 12th Five-Year Plan and in the Period to the Year 2000" emphasize the priority of scientific research devoted to safeguarding the health of the mother and child.

It is now clearly self-evident that safeguarding the health of the mother and child is a problem that is not limited to just a single specialized department. Its solution requires the broad participation of the entire society.

One of the most important comprehensive indicators characterizing the society's living conditions, its public health awareness and the effectiveness of public health is mortality of children in their first year of life.

In the last 15 years, infant mortality decreased significantly in many of the world's countries, by 58 percent in Japan, by 42 percent in the GDR and by a factor of two in Cuba [4,5].

In this same period, infant mortality in our country was characterized by significant fluctuations: Increasing from 1971, it attained 31 deaths per thousand in 1976 [1], after which it began slowly decreasing, and for 8 months of 1989 it has held at 21.7 per thousand. There are a number of general causes responsible for the extremely slow rate of its decline. There is the residual principle of financing public health, the unsatisfactory material and equipment base of public health institutions, and presence of unsolved social problems that affect health. Attainment of child-bearing age by the generation born in the 1960s, when an increase was noted in the country's birth rate, played a role as well. And finally, more complete recording of cases of infant mortality in recent years, especially in rural areas of the republics of Central Asia and the Azerbaijan SSR, should be taken into account.

Significant differences in infant mortality in different republics, cities and rural areas are typical of our country: from 11.3 - 16 per thousand in the Baltic republics, the Ukrainian SSR, the Belorussian SSR and some oblasts of the RSFSR, to 46 - 60 per thousand in the republics and certain oblasts of Central Asia. Consequently, infant mortality is three to four times higher in the Central Asian republics than in other republics.

Infant mortality indicators differ significantly depending on place of residence: In republics with a high mortality, this indicator is 15 - 40 percent higher in the rural population than in the urban population, while in republics with a low level, it is higher in the cities.

In recent years, the AMN SSSR [USSR Academy of Medical Sciences] Pediatrics Institute conducted an integrated study of the causes and factors of infant mortality risk in 10 union republics and four Moscow rayons. Our research revealed a large number of general and regional infant mortality risk factors, which may be divided into three groups—biomedical, social-hygienic, and medical organization [2]. Their influence upon infant mortality is noted in all regions; however, significant differences do exist between them in regard to which particular factors dominate. Thus in regions with high infant mortality, social-hygienic and medical organization factors had the dominant influence on the outcome of disease, while in regions with low mortality, the biomedical factors prevailed.

Biomedical risk factors of infant mortality include extragenital and infectious-inflammatory diseases of the mother, an aggravated obstetric medical history, and the

first delivery by women up to 20 years old suffering disease that is not revealed, in a number of cases, until pregnancy.

Biological risk factors on the part of the fetus and the newborn infant include premature delivery, low body weight at birth, hypoxia, and presence of diseases and background states.

Social-hygienic factors include poor public health awareness of the parents (late referral to a physician concerning a pregnancy or a sick child), inattentive care, feeding and raising of a child, inopportune distribution of family income, an unfavorable psychological climate within the family, and the harmful habits of its members.

Deficiencies in therapeutic and preventive care for the mother and child have an unfavorable effect on the outcome of disease in children in their first year of life. These deficiencies make up the third, so-called medical organization group, of risk factors of infant mortality. Low quality of medical observation of pregnant women in women's consultation offices, a lack of modern examination and treatment methods, improper delivery management tactics, and failure to implement the necessary resuscitation measures and intensive therapy on newborn infants are noted in all places, though at differing frequencies. In the Ukrainian SSR, where infant mortality is relatively low, around 50 percent of infants suffering asphyxiation during birth are not examined after their birth by a neonatologist or an anesthesiologist, not to mention a neuropathologist.

Looking at the stages of care provided to children after release from a maternity hospital, we find poor quality observation of newborn infants, absence of diet adjustment efforts, incomplete examination and treatment of the sick child, and late diagnosis and hospitalization.

The results of our research and materials submitted by our pediatric teams working in the Uzbek SSR show that the extremely unfavorable situation with infant mortality in the region arose in response to many causes. Frequent births, short intervals between them (often less than a year), insensible and insufficient nutrition, and overwork at home and on the job deplete the woman's body and lead to anemia. Seventy percent of pregnant women suffer anemia.

Extragenital pathology was revealed in one of every three women up to 20 years old expecting their first child in the Kara-Kalpak ASSR.

The tradition of blood-relative marriages elicits alarm.

It is children that are born of such marriages that suffer the most severe forms of anemia, hypotrophy, frequent acute intestinal and respiratory diseases, and hereditary diseases.

An inadequate supply of food for children (only 30 - 35 percent of the demand for dairy products, for example) is a large problem in regions with high and average child mortality indicators.

Unsatisfactory supply of water to the population and its low quality should be included in this group of risk factors. For example, almost a third of the population of Surkhan-Darya Oblast is forced to use water from irrigation ditches. Only half of the water pipeline network existing in some areas is equipped with chlorinating devices. There are not enough refrigerators, boiled-water tanks and air conditioners in therapeutic institutions, despite the fact that the country's hottest climate is encountered here. There is no need to prove that these facts play the most important role in creating an unfavorable epidemic situation, one capable of causing an increase and spread of intestinal and other infectious diseases among children. Uncontrolled use of chemical fertilizers that are hazardous to health is a special problem requiring immediate solution.

Insufficient qualifications of the physician should be included among medical organization factors affecting child mortality in regions in which mortality is high. Pediatricians are primarily women, over half of whom are on maternity leave each year. Frequent births mean lengthy interruptions in work, and loss of qualifications. In the Azerbaijan SSR, according to some data, owing to a physician's insufficient qualifications, over 25 percent of dying children had undergone an incomplete examination in the hospital, 36 percent received an incorrect diagnosis, and 50 percent received substandard treatment. An analysis of the causes of child mortality at home and on the first day of hospitalization confirmed the existence of the above-mentioned factors.

In regions with high infant mortality, the laboratory service is in an extremely unsatisfactory state. For example, a number of hospitals of Surkhan-Darya Oblast do not carry out the most highly necessary analyses, even ordinary blood analysis. In the overwhelming majority of cases, children with acute intestinal diseases are not subjected to bacteriological examination to reveal the disease agent, as a result of which they receive inadequate therapy. Training of medical and laboratory assistants is very weak. After graduation from school they are practically unable to work independently.

Special mention should be made of the problem of rural medical care. It is difficult to overstate the role of paramedic-obstetric stations, which are the first, closest and most accessible link of the population to the rural public health system. At the same time, paramedic-obstetric points do not receive the necessary assistance from central rayon hospitals and other higher institutions. The paramedic-obstetric stations do not have telephones and food rations in remote rayons, and they suffer a shortage of transportation resources. All of this results in late detection of disease and hospitalization of patients, and makes it impossible to maintain clear coordination with district and rayon hospitals.

It should be emphasized that shortcomings having to do with medical organization are noted not only in the union republics. Our institute studied the quality of medical care in a number of Moscow rayons. In more

than 50 percent of the cases of sick children receiving substandard treatment, the fault lay with the pediatrician; in 34 percent of the cases the fault lay with inadequate examination; and in 7 percent of the cases the fault lay with parents who were slow to bring their sick children in; in 20 - 25 percent of the cases convalescent patients were not kept under observation, inadequate medicinal therapy was provided, and active house calls were rare.

The results of research by the AMN SSSR Pediatrics Institute show that regional differences exist not only in the causes and risk factors but also in the structure of the causes of infant mortality.

The causes of infant mortality in republics in which it is low are perinatal pathology, developmental abnormalities and respiratory diseases. In regions with high infant mortality, principal among the causes of mortality are respiratory diseases (pneumonia); intestinal infections and sepsis are second, and perinatal pathology is third.

The proportion of neonatal mortality is higher in the cities than in rural areas in all places. Differences in the structure of the causes of neonatal mortality were also noted in this case. In regions with high indicators, first place is occupied by intrauterine hypoxia and asphyxia during labor, after which follow delivery trauma, respiratory disorder syndrome, respiratory diseases and intrauterine infection; when child mortality indicators are low, the causes are the respiratory disorder syndrome, infections, and developmental abnormalities specific to the perinatal period.

Significant regional differences were also revealed in the developmental and nosological structure of infant mortality.

In economically developed countries, the mortality of children in the first month of life makes up 60 - 70 percent of infant mortality. In our country, child mortality at ages above one month dominates in the developmental structure of mortality. The neonatal component is responsible for 20.9 percent in Azerbaijan, 36.6 percent in Kirghizia and 43.7 percent in the Ukraine and Lithuania. It should be emphasized that 45 - 60 percent of all neonatal mortality consists of premature children. A study of the causes and risk factors of premature delivery carried out by our institute in the Estonian SSR, the Kara-Kalpak ASSR and Kaluga Oblast revealed higher perinatal and neonatal mortality among premature children. Thus in the Estonian SSR, perinatal mortality of premature children is 32.7 times higher and neonatal mortality is 17.6 times higher than among children carried to term. These data reveal that the reserve for reducing neonatal mortality rests with its main component—mortality of premature children.

Survival of underweight children, who make up one percent of prematurely born children, is not more than 46 percent; congenital abnormalities are noted three times more frequently among them. Among those who remain alive, 8 - 19 percent suffer gross neurological

disorders and 80 percent suffer other disorders that create problems for the children in school.

Differences in the nosological structure of infant mortality in different regions stem primarily from the level of mortality due to infectious and respiratory diseases.

The following recommendations can be made on the basis of our research

Considering the regional differences revealed in the level, causes, risk factors and structure of infant mortality, prenatal protection of the fetus, resuscitation assistance to children and care of premature children need to be improved in regions with low and moderate infant mortality. Instilling a negative attitude toward abortions, developing contraception and creating a social public health service for families at risk requires special attention in the system for forming a healthy way of life.

Solution of social, ecological and economic problems responsible for the poor health of women and children is the principal condition for reducing infant mortality in regions where its level is high.

Special significance is being acquired by reorganization of therapeutic and preventive care to women and children directed at improving the health of pregnant women, treating the background diseases of children and organizing mobile forms of first aid and the resuscitation service. A family planning service must be created with regard for demographic, national and regional features and traditions.

Thus, integrated research on infant mortality made it possible to reveal the paths and reserves for reducing it. The main and largest reserve is the group of so-called preventable fatal outcomes. These are cases where the deaths of children could have been averted by utilizing current scientific recommendations, given that the work of medical institutions is satisfactory and that the social conditions and public health awareness of the parents are at a sufficient level. Preventable fatal outcomes were from 47.4 to 59 percent in different republics [3] (51.3 percent in the Uzbek SSR for example).

The ways of reducing infant mortality are determined by its causes and facilitating factors. The task is to move, as quickly as possible, the causes into the category of those which can be eliminated, and risk factors into the category of those which can be controlled. We doubtlessly have such possibilities today.

To guarantee this, first of all, the society would have to recognize the problem of safeguarding the health of children as an interdepartmental social problem, one requiring the participation of not only scientists, medical personnel and public health workers, but also the society as a whole.

Second, a regional approach to evaluating the problems and objectives of safeguarding maternity and childhood must be implemented. The question as to the need for a

regional approach to studying the health of children has been examined on several occasions at meetings of the Presidium of the AMN SSSR and the Collegium of the USSR Ministry of Health, at the initiative of the AMN SSSR Pediatrics Institute. This was precisely the approach that was used in research on the causes and risk factors of infant mortality, carried out since 1976 by the AMN SSSR Scientific Research Institute of Pediatrics jointly with other institutes in 10 union republics and in Moscow, and in epidemiological research on pregnancies not carried to term in five economic-geographic regions of the country.

The regional conception of development of the protection of motherhood and childhood is now reflected in comprehensive scientific-practical programs to reduce infant mortality in 1988 - 1995, approved by the USSR Ministry of Health.

We believe that science already possesses sufficiently extensive data on the causes and risk factors of infant mortality, on its regional features and on the ways of reducing it. Were we to include the currently available scientific developments and practical recommendations in long-range comprehensive programs for reducing infant mortality at the level of the republic, oblast, city and rayon, we would be able to eliminate the influence of the principal risk factors, or make them controllable, and significantly reduce infant mortality indicators.

At the same time, the complexity and diversity of the changing social conditions, and of the factors determining the health of the population, raise new problems before medical science or bring to the forefront, ones which we had been aware of before but which had not been viewed as being priority problems. Scientific-Technical Sector Program 0.69.06 and the Five-Year plan foresee solving a number of medical and social problems and going farther in solving the problems of perinatal and infant mortality. The AMN SSSR Scientific Research Institute of Pediatrics is conducting a study of the health of children in one-parent families and in orphanages and developing medical and social measures to improve it in cooperation with the Moscow branch of the Children's Fund. This contingent of children is characterized by high morbidity and infant mortality, exceeding the level in two-parent families by a factor of 2 - 3.

We believe that conducting scientific developments in all directions of the problem of infant mortality, conducting comprehensive research and maintaining a regional approach are the necessary prerequisites for significantly reducing infant mortality in the country.

Bibliography

1. Albitskiy, V. Yu., Vaganov, N. N. and Shchembelev, L. S. "Vsesoyuznaya konf. 'Sotsialno-gigiyenicheskiye problemy pediatrii', 2-ya Tezisy dokladov" [All-Union Conference "Social and Hygienic Problems of Pediatrics", 2d: Report Abstracts]. Minsk, 1989, pp 3-4.

2. Studenikin, M. Ya., *PEDIATRIYA*, No 2, 1986, pp 3-8.

3. Studenikin, M. Ya. and Temicheva, L. S., "Vsesoyuznaya nauch.-prakt. konf. 'Sostoyaniye zdorov'ya i puti povysheniya kachestva lechebno-profilakticheskoy pomoshchi zhenshchine-materi i rebenku': Tezisy dokladov" [All-Union Scientific-Practical Conference "Health and the Ways of Upgrading the Quality of Therapeutic and Preventive Care for the Mother and Child": Report Abstracts], Moscow, 1987, pp 100-102.

4. Cortequere, R. R., Muniz, J. A. G. et al., *BOL. OFIC. SANIT. PANAMER.*, Vol 92 No 5, 1982, pp 379-390.

5. "The State of the World's Children 1988," pp 64-65.

COPYRIGHT: Izdatelstvo "Meditsina", 1990

Program for Reducing Infant Mortality in the Uzbek SSR

917C0085C Moscow VESTNIK AKADEMII
MEDITSINSKIH NAUK SSSR in Russian No 7,
Jul 90 pp 10-12

[Article by S. M. Bakhramov]

UDC 616.053.31:312.2(575.1)

[Text] It would be impossible to implement a program to safeguard the health of the child population and reduce infant mortality without accounting for cause-and-effect phenomena determined by the socioeconomic standard of living, public health awareness, the state of the biosphere, demographic features and public health care. Only objective analysis of the sum total of these phenomena can aid us in correctly determining the strategy and tactics of reducing infant mortality.

The high infant mortality presently existing in Uzbekistan, which is only just beginning to acquire a decreasing trend, is a natural consequence of the effect of a complex of negative factors which evolved in the region over a long period of time.

A high proportion of children in the population (40 percent), a high birth rate and a tendency for large families on the backdrop of a low standard of living are among the demographic and socioeconomic features of the republic, two-thirds of the population of which is rural. Almost a third of the country's large families live in Uzbekistan. Optimum intervals between pregnancies are observed among 50 percent of the women, while 12-14 percent of them have children twice a year. Fourteen percent of marriages are between blood relatives. Over 40 percent of rural families have a per-capita income of less than 40 rubles. Around 200,000 women work in unfavorable conditions, with around 10,000 of them employed in heavy physical work.

An ecologically unhealthy situation has evolved in Uzbekistan, especially in the Aral region. Over 80 percent of the republic's state water mains and more than 60 percent of its departmental mains do not satisfy sanitary engineering requirements. Centralized water supplies are available to 79.4 percent of the urban and only 48 percent of the rural population.

Under residual financing of public health, not more than 4 percent of the budget was allocated in the country as a whole to 25 percent of the child population. In the Uzbek SSR, where children make up 40 percent of the population, the negative consequences of this are felt especially strongly. Today only 16 percent of children's institutions and 30 percent of maternity hospitals are housed in standard buildings; the rest are in makeshift buildings that now require overhaul and remodeling. The state of infection hospitals raises special alarm: 70 percent of them are in makeshift buildings, 90 percent have no sewage systems, 65 percent have no hot water, and around 20 percent have their water trucked in. Over 60 percent of rural district hospitals, paramedic-obstetric stations and outpatient clinics are also located in makeshift buildings.

There is a shortage of 9,000 obstetric-gynecological beds in the republic, the availability of children's beds is 75 per 10,000 (compared to a norm of 113.7), the availability of children's beds in infectious wards is 20.1 (compared to a norm of 36.9), the availability of neonatal beds is 2.5 (compared to a norm of 5.7), and so on.

There are 14 pediatricians per 10,000 children in the republic (compared to a norm of 20.5), and there are 2.2 obstetrician-gynecologists per 10,000 adults.

Over 20 percent of the paramedic-obstetric stations are not staffed with obstetricians, while over 60 percent are not staffed with public health nurses. Only around 13 percent of the pediatricians and 29 percent of the obstetrician-gynecologists possess the appropriate qualifications. Each year over 17 percent of the physicians and more than 20 percent of the nurses are not working for reason of maternity leaves and caring for young children. These are the reasons for the personnel shortage and the substandard quality of medical personnel. The factors listed above cannot help but have an effect upon the health of women and children, and ultimately on infant mortality.

Each year over 34,000 premature children are born in the republic, and over 90,000 physiologically deficient children are placed under the observation of pediatricians.

The unsatisfactory state of public health in population centers, unfavorable ecological changes and the low public health awareness of a part of the rural population have created a situation in Uzbekistan where hepatitis morbidity exceeds the union average by four times and the incidence of typhoid fever exceeds the union average by three to four times. A similar pattern is observed in relation to some other intestinal infections.

In rural areas, 75 percent of children in their first year of life suffer an aggravated pre-morbid state (malnutrition, rickets, anemia, exudative-catarrhal diathesis). The unbalanced diet received by nursing children has an unfavorable effect on their health. From 25 - 60 percent of children of early age are provided formula. The Ministry of Trade satisfies 50 percent of the demand for powdered milk and other baby food products in the republic, and 20 percent of the demand for canned meats for children (200,000 - 250,000 standard cans).

Analysis of infant mortality in the republic in the 3 years of the 12th Five-Year Plan revealed certain age-related and structural features, and its dependence upon the frequency of births and season. Of the number of children dying before one year of age, almost a fifth die in maternity hospitals. Infant mortality was observed to be especially high in maternity hospitals of Fergana, Samarkand, Syr-Darya, Bukhara and Tashkent oblasts and in the Kara-Kalpak ASSR. More than half of children dying in the postnatal period do so during the first half year. Short intervals between pregnancies and frequent births have created a situation where 21 out of 1,000 first-born children die, while 23 second children and 43 fourth and subsequent children die. Among children dying in the first year of life, around 80 percent suffered an aggravated pre-morbid state. One-fourth of all children that died possessed developmental abnormalities and perinatal pathology. Among diseases causing the death of children, diseases of the respiratory system, including pneumonia, occupied first place, intestinal infections were second, and perinatal pathology was third. Almost 40 - 50 percent of the children that died in rural hospitals did so within a day. Mortality also remains high among children born at home.

Socioeconomic measures are being conducted in the republic and its biosphere is being improved in accordance with general state and directive acts, as well as in accordance with the decree of the CPSU Central Committee and the USSR Council of Ministers on the Aral. In order to intensify state public health supervision over the supply of high quality drinking water to the population by the Uzbek SSR Ministry of Health and Ministry of Housing and Municipal Services, public health measures aimed at bringing all substandard water mains up to a condition satisfying sanitary engineering requirements were drawn up. The Uzbek SSR Council of Ministers formed a republic commission to improve the supply of high quality drinking water to the population, and it developed a comprehensive program which will make it possible to completely satisfy the demand of the republic's population for drinking water by the year 2000.

The epidemiological services have begun monitoring enterprises that pollute the environment and are involved in food production more strictly.

In accordance with a comprehensive regional program to protect motherhood and childhood, each year around 50,000 mothers undergo a health improvement course in

142 sanatoriums and preventive hospitals, in five "Mother and Child" hospitals, in day hospitals possessing a total of 300 beds, and on 3,500 specially allocated therapeutic beds. In addition, therapeutic departments have allocated beds to be used by pregnant women with extragenital diseases for up to 28 weeks, and for the treatment of women with pregnancy-related pathology. Maternity hospitals have been specialized in Tashkent for women with cardiovascular pathology, with Rh-factor conflict, and women suffering tuberculosis and toxic-septic infection. Twelve interrayon hepatitis departments containing 1,100 beds were organized for the treatment of women in childbirth who have contracted viral hepatitis. An additional 3,488 obstetrician positions were created by a decree of the Uzbek SSR Council of Ministers dated 9 April 1986 in order to improve public health care to pregnant women in rural areas. Children's gynecological offices were organized in children's polyclinics of Tashkent and Bukhara. Gynecological beds were allocated for children and adolescents by the Scientific Research Institute of Obstetrics and Gynecology of the Samarkand Medical Institute.

Family planning has a direct bearing on the health of women and on reducing maternal mortality, perinatal morbidity and infant mortality. In this connection the republic's Ministry of Health developed a complex of interdepartmental measures directed at altering the sexual behavior of women. In order to permit purposeful preventive work in the republic's oblasts, 35 additional official units were approved and the position of chief supernumerary contraception specialist of the Uzbek SSR Ministry of Health was introduced. A family planning department was created under the Scientific Research Institute of Obstetrics and Gynecology. This department develops scientific recommendations and provides practical assistance in creating the corresponding services in each oblast. Three republic conferences on the medical aspects of family planning were conducted.

Demographers, economists and sociologists, who will help to resolve not only medical but also many socioeconomic issues, will take part in the republic program on this problem. This program is financed by the republic's Lenin Fund, for which we express our deep gratitude.

A republic consultation office of medical genetics was organized under the Scientific Research Institute of Obstetrics and Gynecology and five offices were created in the oblasts in order to reveal and prevent hereditary diseases. A "Marriage and Family" office is functioning in Tashkent in the children's consultative and diagnostic polyclinic.

A certain amount of work was done during the 12th Five-Year Plan to improve children's public health. The republic possesses 62,200 beds for hospital care in 10 children's oblast hospitals, 48 city hospitals, 19 specialized hospitals, 8 rural hospitals, in central rayon hospitals, and in clinics run by scientific research institutes and medical schools.

Outpatient and polyclinic care is provided in 1,660 children's polyclinics and consultation offices, where physicians in 4 - 18 specialties hold office hours.

Republic children's centers for allergiology, pulmonology, surgery, ophthalmology, endocrinology and pathology of young children and premature infant care centers have been created at the leading children's hospitals, scientific research institutes and medical school departments. They serve as training and consultative centers at which pediatricians and middle-grade medical personnel upgrade their qualifications.

Special attention is being devoted to developing and improving the neonatal service. Departments of premature infant care and infant pathology were organized in Tashkent and in oblast centers, and neonatal wards have been specialized in a number of oblasts. The number of beds for sick infants and premature infants has been doubled, and steps are being taken to organize inter-rayon departments. Nineteen resuscitation departments have been organized in maternity and children's hospitals.

Five hundred sixty-five medical and paramedic teams, including 13 resuscitation and three neonatal, now provide first aid and emergency care to children.

In the outpatient and polyclinic service, attention is being devoted mainly to children in the risk group and children from socially troubled families. A system of differentiated observation of such children is being introduced and new forms and method of work (micro-districts, neonatal districts, a one-pediatrician system etc.) are being utilized for this purpose. Efforts are being made to reduce the size of pediatric districts. The average number of patients per district in the urban environment is 860 - 900 (the ages of 60 - 80 of these patients are from 0 to 1 year), which makes it possible to improve the health of children and prevent disease better. In 1988, 83.5 percent of children in their first year of life were under the systematic observation of a physician.

An additional 3,802.5 public health nurse positions were introduced into the manning of paramedic-obstetric stations. Instructions of the Uzbek SSR Council of Ministers, dated from 14 March 1988 to 1 April 1988, recommend introducing a junior nurse position into the staff of paramedic-obstetric stations at profitable kolkhozes and sovkhoses, and at their expense, in the Kara-Kalpak ASSR and in Samarkand, Bukhara, Kashka-Darya and Surkhan-Darya oblasts, where infant mortality is high. However, because of the absence of financing, only 290 of the 689 trained nurses are currently working.

Provision of baby food to low-income and large families free of charge has been organized. In comparison with 1987, allocations for free food for children up to 2 years old were increased eight-fold (to 6 million rubles), in 1989 they were increased to 7.8 million, and in 1990 12 million rubles are to be allocated. However, up to 70

million rubles need to be allocated yearly in order to satisfy the demand completely.

There are plans for producing 15,000 tons of vitamin-enriched milk, 4,000 tons of strained foods, 80 million standard cans of canned goods and 1,000 tons of sausage of standardized nutrient content in the republic in 1990 in order to satisfy the demand for children's food.

Considering the need for priority development of the motherhood and childhood protection service, in the 12th Five-Year Plan the republic's Ministry of Health is allocating 30 - 40 percent of capital investments to children's and maternity facilities. In 1987, around 60 percent of the beds that were placed into operation were in pediatric and obstetric-gynecological wards. One hundred eighty-four administrative buildings were transferred to the needs of children's public health. Allocations to public health will increase dramatically in 1988—1.2 billion rubles, which is 10 percent of the republic's budget. There are plans for organizing 69,200 children's beds, including 26,400 in infectious wards, by 1995.

A significant effort has also been made to prevent morbidity and reduce infant mortality in the summer months. Oral rehydration stations are being deployed and house-to-house inspection rounds are being expanded in all polyclinics of rural district hospitals and paramedic-obstetric stations during the period of higher incidence of acute intestinal infection. Teams of physicians and medical school and institute students are traveling to the rayons, and the instructor staff is being mobilized. Medical teams of the USSR Ministry of Health are providing considerable assistance. Not only do they render medical and organizational assistance, but they also provide advanced training to physicians locally. Teams of physicians certified by the All-Union Children's Fund imeni V. I. Lenin, who are the chief specialists of the USSR Ministry of Health, are also taking an active part in these efforts. Besides printed materials, public health education makes use of radio and television, and seven short films are currently being produced in Uzbek and in Russian.

Pediatricians and obstetrician-gynecologists are receiving advanced training in the Tashkent Institute for the Advanced Training of Physicians, at medical school departments for advanced training, and at work stations in scientific research institutes. More than 25 seminars and conferences on various subdivisions of pediatric medicine have been conducted for the republic's pediatricians by the efforts of a number of medical schools at the invitation of the Uzbek SSR Ministry of Health.

Such is far from a complete list of measures being implemented in the Uzbek SSR in the 12th Five-Year Plan in the program to reduce infant mortality. But the practical results in three years of the Five-Year plan are extremely modest. We were able to stabilize maternal mortality. The frequency of premature births has decreased somewhat, as has infant mortality in general.

It is naturally impossible to quickly correct the unfavorable situation that has evolved in the republic in safeguarding maternity and childhood. We are aware that a long and difficult effort still awaits us. The positive changes that have occurred in the consciousness of the society in this direction, and not only the moral but also the material support of party and soviet organs, will ultimately make it possible for medical workers to reach this objective.

COPYRIGHT: Izdatelstvo "Meditsina", 1990

Causes of the Death of Children in Their First Year of Life in Rural Uzbek SSR

917C0085D Moscow VESTNIK AKADEMII
MEDITSINSKIH NAUK SSSR in Russian No. 7,
Jul 90 pp 13-15

[Article by I. R. Klibley, M. U. Nizamova and O. A. Pugacheva, Scientific Research Institute of Pediatrics, Uzbek SSR Ministry of Health, Tashkent]

UDC 616.053.31-036.88-02(575.1-22)

[Text] The program for improving protection of the health of the mother and child has been recognized as being one of the priority directions in the development and restructuring of public health in the period to the year 2005. It is acquiring especially important significance in the Uzbek SSR.

A high birth rate, a large proportion of children in the population and high infant mortality characterize the demography of the Uzbek SSR in relation to public health. Infant mortality is an indicator of the population's health and its material and cultural state. It is associated to a significant degree with the health of parents, with the conditions in which the child lives and grows, and with the level and quality of therapeutic and preventive care provided to women, newborn infants and children up to one year old.

A large effort is being made in the republic to improve medical services to the entire population, including pregnant women, nursing mothers and children. Owing to preventive measures, a tendency for infant mortality to decline has been noted in Uzbekistan. In 1988 this indicator was 43.3 per thousand, as compared to 45.9 per thousand in 1987 and 46.2 per thousand in 1986. It remains high, however: It exceeds the country average by a factor of 1.6 and the average in other republics (the Ukraine, Belorussia, RSFSR) by a factor of 2 - 2.5. It should be pointed out that the birth rate in the Uzbek SSR (37.0 in 1987, 35.4 in 1988) is one and a half times greater than the average for the USSR (21.7); half of all of the population is made up of children aged from 0 - 14 years, among which 45 percent are being raised in large families with four or more children.

High infant mortality is observed in the republic's rural areas, especially in the south, in Surkhan-Darya Oblast, which possesses unique climatic, demographic, social

and biological features. In this connection, the age-related and nosological structure of the population was studied for three years (1986 - 1988) with regard for the entire complex of local factors in order to arrive at effective measures by which to reduce infant mortality in the oblast.

More than 900 deaths of children up to one year old, divided into age groups of up to 1, 1 - 3, 3 - 6, 6 - 9 and 9 - 12 months, were subjected to expert assessment. The research results show that infant mortality exhibits unique features in different periods of the first year of life [7]. Children die mostly in their first week of life and at ages from 1 - 6 months. Thus, in the three years, of all children that died at ages up to one year, 32 percent did so in the neonatal period, including 66.5 percent in the first seven days of life.

Analysis of representative data on children born alive in maternity hospitals and dying at ages of up to one year, and children surviving up to one year, revealed that 19 - 25 percent of women in rural areas give birth twice a year; there is a high percentage of marriages among blood relatives (21.6 percent); 35 - 39 percent of births are by women who have borne many children; there is a high proportion of mothers with extragenital diseases (35.7 percent) and with complicated pregnancies (29.8 percent) which lead to complications in delivery and to pathology of newborn infants [6]. It should be considered that a significant percentage of these women are employed in jobs failing to meet public health standards. Clinical examination and treatment of women of child-bearing age and pregnant women is unsatisfactory; only 32.4 percent of pregnant women regularly visit women's consultation offices.

The complex of factors presented above is responsible for the birth of a large number of children (37.85 percent) exhibiting phenomena of perinatal pathology. The causes of death of newborn infants in the early neonatal period are as follows: hypoxic states, birth trauma, developmental abnormalities, pneumonia, and toxic-septic diseases [5]. In the late neonatal period (7 - 28 days), children died of acute intestinal infections, respiratory diseases, hemolytic disease and developmental abnormalities. Moreover, a large proportion of the children died in the first 10 days after release from the maternity hospital—that is, they were released under the observation of a district pediatrician despite the fact that they should have been transferred to infant pathology departments. These causes of death among children in the neonatal period are directly dependent on factors having to do with the organization of medical care—absence of modern infant pathology departments, low qualifications of obstetrician-gynecologists and neonatologists, and poor availability of materials and equipment at maternity hospitals and in children's departments of central rayon hospitals in rural rayons of Surkhan-Darya Oblast. Medical organization factors are controllable; they depend not only on the qualifications of physicians and on availability of materials and equipment, but also on the promptness of therapeutic and

preventive care and the conscientiousness of medical workers. Analysis of preventive care rendered to newborn infants in outpatient and polyclinic institutions revealed that the quality of public health observation of pregnant women and children by district pediatricians and middle-grade medical personnel suffers in all cases [1]. Thus, public health service was not provided at all to newborn infants in the first three days after their release from the maternity hospital. In 25 percent of the cases the pediatrician visited the newborn infant on the 6th - 10th day after release, and over half of the newborn infants that died had not been examined by a district physician a single time during their entire first month of life. The research results show that absence or untimely public health service to newborn infants increases infant mortality by a factor of over 2 - 3.5 [3].

Sensible feeding during the first year of life has especially great significance to proper development of the child. In Central Asian republics, and especially in rural areas, the number of breast-fed children is still rather high. However, the fact that the observed tendency for the frequency and duration of breast feeding to decline in Surkhan-Darya Oblast elicits a certain amount of concern. The number of newborn infants maintained by artificial feeding from the day of their birth (8.6 percent) is increasing. Up to 20 percent of children are switched to artificial feeding at an age of one month, while over half are maintained by mixed feeding at ages of 1.5 - 2 months; infant mortality among artificially fed children was 2.5 times greater than among children maintained by natural feeding [2].

The principal causes of death in the age group of children from one month to one year was infectious-parasitic diseases, respiratory diseases, and some forms of perinatal pathology. The unique features of the republic's southern oblast include the highest relative incidence of acute intestinal infections and the highest infant mortality due to this pathology.

Presence of an aggravated pre-morbid state in children, shortcomings in the efforts by outpatient and polyclinic institutions to organize sensible feeding, the poorly developed network of dairy kitchens and the inadequate supply of powdered and canned foods for children in rural areas created the background for growth of the incidence of gastrointestinal diseases of alimentary and combined alimentary-infectious origin. This is why 72.8 percent of children who died at an age of up to one year suffered an aggravated pre-morbid state, while infant mortality in this group was 2.1 times higher than among children without this pathology [4].

In Uzbekistan's oblasts, fluctuations in infant mortality depend on time of year, and they are associated with climatic and geographic features. In the south (Surkhan-Darya Oblast), two highs can be noted in infant mortality—summer-fall and winter-spring. The summer high is the product of a high level of gastrointestinal diseases, and it is especially typical of rural areas. In winter, the high is the product of high morbidity and mortality due

to pneumonia. Unsatisfactory organization of therapeutic and preventive care has an effect on infant mortality. In a number of cases, deficiencies in medical service to children prior to entering the hospital are the result of the fact that in most cases parents in rural areas wait too long to go to paramedic-obstetric stations when their children are sick. Moreover, the stations are staffed with middle-grade medical personnel who are not always able to correctly assess the condition of children. The unsatisfactory material base of children's hospitals, a lack of successiveness in hospitalization procedures, and the absence of children's resuscitation departments facilitate cross infection of sick children and raise mortality. Thus out of all children dying at ages up to one year in the oblast, 25.2 percent died at home, without medical care, while the rest died in hospitals, with 37.6 percent of them dying on the first day of hospitalization.

The main causes of death at home are the parents' refusal to hospitalize their child (24.6 percent), untimely referral to a physician (35.2 percent) and understatement of the condition of the child by medical workers (26.2 percent). The causes of death of children on the first day of hospitalization were late hospitalization (32.1 percent), absence of timely resuscitation (37.9 percent) and low qualifications of attendant physicians (15.9 percent) [3].

Social factors, such as the educational level of parents, their health, material welfare and housing conditions, the mother's family status, the number of children in the family and alcohol abuse by the parents have significant influence on infant mortality [2,3].

As a rule, these factors act in combination. All cases of the death of children in their first year of life may be subdivided in relation to their causes into preventable and unpreventable. We characterized as unpreventable mortality (29.7 percent) those cases in which the present level of medical science and organization of ideal care are unable to exert a positive influence. Preventable mortality (60.1 percent) includes those cases in which death occurred due to diseases that may have been successfully prevented or treated, had the necessary steps been taken.

Risk factors having a dependable and significant influence on infant mortality (medical, organizational, social, biological) were isolated and a table by which to make individual evaluations and predictions of the risk of death of children in their first year of life was compiled on the basis of our data. The leading risk factors for Surkhan-Darya Oblast today are medical-organizational (45 percent) and social-hygienic (32.6 percent). However, the effect of these factors differs in each age group. Thus, medical, biological and organizational factors have greater influence on neonatal mortality, while post-neonatal mortality is dependent first on medical-organizational factors and then on social-hygienic factors [1,7].

An unhealthy way of life of the parents and certain shortcomings in the organization of medical services to children have a significant unfavorable influence on infant mortality on the first day of hospitalization and outside the hospital. Thus our research revealed the risk factors affecting infant mortality, and they made it possible to predict the death risk in each specific case and propose measures to reduce infant mortality.

Bibliography

1. Akhmetova, G. Kh., ZDRAVOOKHR. KAZAKHSTANA, No 7, 1980, pp 16-20.
2. Gamidov, F. A., ZDRAVOOKHR. ROS. FEDERATSII, No 8, 1967, pp 15-19.
3. Zubritskiy, M. K., ZDRAVOOKR. BELORUSSII, No 3, 1969, pp 66-69.
4. Kalancha, R. N., SOV. ZDRAVOOKHR., No 4, 1980, pp 45-48.
5. Rakhmatulina, V. G. and Rozhkova, P. A., "Aktualnyye problemy spetsializirovannoy pomoschi detyam" [Pressing Problems in Specialized Care for Children], Kuybyshev, 1979, pp 57-58.
6. Titova, V. V., "Pathology in the Period of Infancy in Some Cities of the Uzbek SSR", Abstract of a dissertation in pursuit of the academic degree of candidate of medical sciences, Tashkent, 1989.
7. Usmanov, Ya. U., "Causes and Factors Determining the Health of Children in Their First Year of Life in the Kara-Kalpak ASSR", Abstract of a dissertation in pursuit of the academic degree of candidate of medical sciences, Moscow, 1985.

COPYRIGHT: Izdatelstvo "Meditsina", 1990

Concomitant Radiation Effects, Their Immediate and Remote Consequences

917C00584 Moscow TERAPEVICHESKIY ARKHIV
in Russian Vol 62 No 7, Jul 90 pp 11-15

[Article by Ye. Ye. Gogin]

UDC 617-001.28-06-036.8

[Text] The disaster at the Chernobyl Nuclear Power Plant, which was the most serious of all disasters that have occurred to date involving the peaceful use of atomic energy, but which was far from the worst possible, took the lives of 30 people and caused 200 to suffer acute radiation sickness (ARS). But there is more to the consequences of this tragedy than this. A number of medical problems have arisen. Some of them have to do with the acute period of the disease elicited by exposure to radiation, and are important to an understanding of the peculiarities in the course of radiation injury and to the use of accumulated experience in the future. Others pertain to the remote consequences of radiation exposure and to the influence of small doses associated with practically constant exposure of the individual to radiation. These problems must be solved in the interests of victims and people residing in a number of Belorussian and Ukrainian rayons, and in neighboring RSFSR oblasts, characterized by an elevated radiation background.

The consequences of radiation injury are not limited to development of ARS or chronic radiation sickness (CRS) (ARS occurs with short-term and CRS occurs with long-term or recurrent exposure). In the case of local (or predominantly local) exposure at certain doses, radiation burns arise or the function of some organ is disturbed, for example, the thyroid gland when radioactive iodine is incorporated. A special distinction is made between the genetic consequences and the carcinogenic action of ionizing radiation.

Once clinical consequences of exposure to ionizing radiation, which do not provide the grounds for a diagnosis of radiation sickness, exist and the concept of radiation sickness does not encompass the entire spectrum of consequences of radiation injury, we must then mark out the boundaries of ARS and determine the forms of injuries and processes which are outside these boundaries.

Radiation sickness is defined in the Medical Encyclopedia as "a disease elicited by exposure of the organism to ionizing radiation in doses exceeding maximum permissible limits". But then it goes on to say that "acute radiation sickness or the acute radiation syndrome...arises in response to relatively short-term exposure to a total dose exceeding 1 J/kg (100 rad)" [4]. If we consider that 5 rad per year is the maximum permissible dose for people working with sources of ionizing radiation (category A), that 0.5 rad is the maximum for category B, and that 0.05 rad per year is the maximum for the population

as a whole (category C), there remains no doubt that no similarities exist between the concept ARS (or acute radiation syndrome) and the broader concept of pathogenic radiation exposure [1,11,14].

A. V. Barabanova, A. Ye. Baranov, A. K. Guskova et al. use the term ARS as an umbrella for "the group of syndromes developing after short-term exposure of the whole body or a larger part of it to a dose of more than 0.5 - 1.0 Gy (50 - 100 rad), with the mandatory presence of signs of suppression of hemopoiesis and a limit of 2 - 3 months for all of the basic pathological changes to occur" [23].

This wording imposes rigid boundaries upon the use of the term ARS, and doubtlessly simplifies diagnostic practice and the conclusions reached through it by physicians and expert commissions. It is based on three *a priori* premises:

1. At exposure doses less than 50 rad, ARS cannot arise under any circumstances; any consequences of such exposure cannot be qualified as ARS.

2. If signs of suppression of hemopoiesis are absent, ARS cannot be diagnosed; the objective laboratory (hematological) criterion is rendered absolute in this way. This is valid in relation to the bone marrow form of ARS and forms associated with it, but strictly speaking, it leaves its fastest-progressing variants, and particularly the cerebral form, or the instant form, in which the signs of suppression of hemopoiesis simply do not have time to appear outside the framework of ARS. The radiation consequences of local exposure and small exposure doses are cut off just as decisively.

3. Although limiting the time for occurrence of the principal pathological changes to a period of 2 - 3 months does follow from routine clinical experience and corresponds to the definition itself that a radiation syndrome is acute if it follows one-time exposure, it cannot be accepted unquestioningly either, especially in cases of concomitant exposure. Two of the victims of the disaster at the Chernobyl Nuclear Power Plant died more than 2 - 3 months later. This means that the basic pathological changes had not yet run their course by this time [12]. Moreover there are other "secondary" pathological changes that cannot fit within the 2 - 3 month time frame. Let me cite a case in which the leg of a young man, suffering the severe form of ARS, had to be amputated 4 months after exposure due to an infected, nonhealing ulcer that arose on his lower leg as a result of a radiation burn [9].

Therefore despite the pragmatic value of the proposed definition of ARS, it must be kept in mind that it leaves forms of radiation pathology not corresponding to this definition outside the rigidly identified boundaries of ARS. The proposed wording makes examination of other forms of radiation pathology urgently necessary. The authors of the cited document also offer a definition for the concept of local radiation injury: "Pathological changes in tissues of a limited portion of the body,

arising after short-term exposure of the body to ionizing radiation at a dose of more than 8 - 10 Gy, are identified by the term acute local radiation injury—ALRI." There is no need for examining this definition in as great a detail as that of ARS, but it is obvious that if ALRI involves significant volumes or surfaces (in the case of predominant skin injury), as with any kind of burn it necessarily leads to a certain reaction on the part of the entire organism; there is good reason why the concept of "burn disease" has justifiably come into its own right. In cases of real radiation injury of an individual in accidents, and especially within the zone of release of radioactive noble gases in aerosols and in the track of a radioactive cloud, not only will ARS and ALRI always be concomitant and coincident in time of development, but they will also exist in a certain proportionate dependence, because the doses of penetrating radiation components and the doses of highly absorbable components depend equally not only on the composition of the mixture but also on its concentration [15]. Therefore it would be proper to look at ARS and ALRI separately in victims in these cases. The sole correct conception is that of ARS arising from concomitant radiation injury. No matter what manifestations of ARS and ALRI we examine, their formation, depth and dynamics will be found to be dependent not on just one of these factors but on the integral effect of both, and they will mutually aggravate the course of disease [9,10].

Even in the classical cases of the bone marrow form of ARS, in addition to the direct injury of the most radiosensitive bone marrow cells determining the course of illness, the sum total of effects of ionizing radiation on other organs and tissues acquired important significance [2]. The more nonuniformly the absorbed doses are distributed and the more pronounced the shielding effect on at least part of the hemopoietic tissue was expressed, the greater the contribution made by the ALRI component to development of ARS [19]. In the case of ARS caused by concomitant exposure to an atmosphere of radioactive noble gases and ash from accidents, the nonuniformity of doses expresses itself as widespread, clinically manifested skin injury [21]. In other cases a higher proportion of injury to tissues other than bone marrow leads to the intestinal, toxic or cerebral form of ARS.

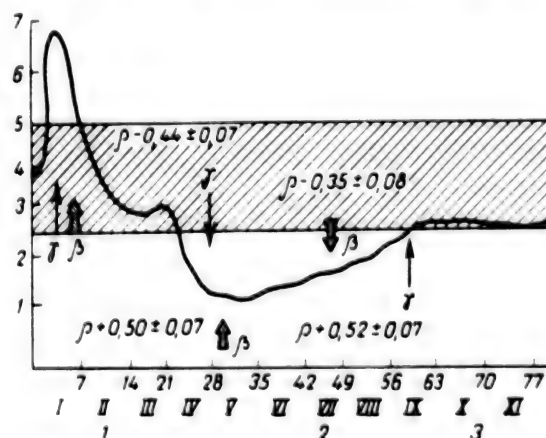
The experience of treating victims at the Chernobyl Nuclear Power Plant disaster revealed quite obviously that "the overall course of disease is characterized by significantly greater expressiveness of the endogenic intoxication syndrome; injuries to the skin and soft tissues of the limbs and the mucus membranes of the mouth and throat acquire important significance" [23]. As a rule the outcomes are "more severe with a relatively lower degree of suppression of hemopoiesis than is observed with uniform exposure" [23], but specialists have refrained from the use of the term "ARS accompanying concomitant radiation injury" and from making conclusions concerning the protracted course of the recovery period of these patients, amplification of their

residual defect and growth of the probability of an unfavorable outcome of illness, both immediate and remote.

There is special interest in analyzing the effect of ALRI on one hand and the direct influence of penetrating radiation components affecting bone marrow tissue on leukopoiesis indicators and on the granulocyte count in peripheral blood on the other, inasmuch as this is one of the quantitative indicators used as a criterion of the severity of ARS [3,6-8,24-27].

The extremely complex radiation situation at the Chernobyl Nuclear Power Plant accident would not permit assessment of the contribution of each of the radiation components to the injurious effect; however, this was done in an examination of a large group of light casualties (first degree ARS and subclinical forms of acute radiation injury) in 1961. It was possible then to calculate individual doses of gamma-radiation, and the beta-exposure ratios for each of the subjects could also be estimated from the magnitude of inhalational accumulation of radioactive iodine by the thyroid. It was established that on the 21st - 30th days after exposure, when the decline in the neutrophil count was the most significant (radioactive depression of the granulocyte precursor in bone marrow hemopoiesis), the coefficient of correlation between the individual dose of gamma-radiation and the neutrophil count was equal to -0.44 ± 0.07 ($p < 0.01$), and that the coefficient of partial correlation between the concentration of ^{131}I and the neutrophil count was $+0.50 \pm 0.07$ ($p < 0.01$; see figure).

Thus, local radiation burns were found to have a directly opposite effect on the level of hemopoiesis than that of



Coefficients of Partial Correlation (ρ) of the Exposure Doses of Gamma- and Beta-Radiation and the Neutrophilic Leukocyte Count in Peripheral Blood ($1-7 \times 10^9/\text{liter}$) at Different Times After Concomitant Radiation Injury in Light Casualties: abscissa—first row of numbers—days, second—weeks, third—months; ordinate—neutrophilic leukocyte count

radiation exposure of bone marrow per se; in this case, the larger the exposure dose was, the more distinctively the neutropenic effect prevailed. At general gamma-radiation exposure doses less than 30-35 R, neutropenia did not arise, irrespective of the initial hemopoietic situation, while at doses greater than 100 R it was significant no matter what the individual sensitivity of the victim and the volume of local injury. But at doses of 40-95 R a decrease in neutrophil count was noted only among persons with relatively low leukocyte indicators prior to radiation injury.

During the second month after exposure, when in the case of first degree ARS the neutrophilic leukocyte count is known to recover from isolated gamma-radiation exposure, the correlation between the gamma-radiation exposure doses of the victims of concomitant exposure and the volume indicator of local radiation effect on one hand and the neutrophil count on the other was no less significant, but the influence of each of these factors was found to be oppositely directed by this time: The coefficient of partial correlation with the gamma-radiation exposure dose assumed a value of $+0.52 \pm 0.07$, while with accumulation of ^{131}I , it assumed a value of 0.35 ± 0.08 ($p < 0.01$). Thus a decrease in the rate of normalization of the neutrophil count was the consequence of the effect of the mild components of irradiation in the period of recovery of hemopoiesis.

The influence of local radiation injury on the acute radiation syndrome of the victims of concomitant radiation injury, which was mutually aggravating in the recovery period and masking in the period of development of the acute radiation syndrome, was proven mathematically in the clinical observations described above. It is well known that radiation injury of organs and tissues, and radiation burns in particular, have a specific influence on the functional state of hemopoietic bone marrow. Optimally, this influence stimulates granulocytopenia in response to the advent of inflammation foci in the organism that generate a demand for larger numbers of leukocytes. The so-called colony stimulating factor (CSF), which has not only been chemically identified but is already being industrially produced in the form of a medicinal preparation, has the dominant significance in this system. The first attempts at therapeutic use of CSF on irradiated patients have been made.

Examining the cause-and-effect relationships at the basis of the mechanism of the influence of local radiation injury, and particularly of skin burns, on bone marrow hemopoiesis in the case of concomitant exposure of the individual to radiation, we can conclude that the CSF plays the leading role. When direct radiation injury of bone marrow tissue is moderate, this can lead to a masking or possibly even a compensatory effect, to reduction of granulocytopenia, while at greater volumes of evacuation of bone marrow the possibility is not excluded that the CSF would have a negative influence. In the absence of functionally active myelopoietic cells, it worsens the situation.

Development of the radiation syndrome differs fundamentally depending on the time of exposure, its intensity and its constancy [16,17,20,22], despite the fact that the primary biophysical effects of exposure to ionizing radiation are identical. ARS does not transform into CRS—these are two completely isolated nosological forms [13]. However, this difference does not mean that ARS runs its course without consequences. Certain disorders, dysfunctions and residual changes creating a postradiation defect or an asthenovegetative syndrome or a pre-morbid complex of subsequently developing nonspecific illnesses often persist or manifest themselves following the recovery period of ARS.

Evaluating the persistent consequences of acute concomitant radiation injury, let me cite my own observations once again. A group of young men who had suffered first degree ARS were examined during the acute period of disease, and then two and three years after exposure. The rate of propagation of a pulse wave through vessels of predominantly muscular type (V_m) increased in them from 690 ± 16 to 763 ± 17 cm/sec at different stages of the acute period of disease, to 802 ± 38 cm/sec two years later and 819 ± 19 cm/sec three years after exposure, while the rate of propagation of a pulse wave through vessels of the elastic type (V_e) increased from 553 ± 10 to 587 ± 11 cm/sec in the period of disease, to 695 ± 32 cm/sec two years after exposure and 661 ± 15 cm/sec three years after. If we consider that, according to mechanocardiographic data obtained for men by N. N. Savitskiy's method, V_e is equal to 600 cm/sec at ages 21-30 years and 714 cm/sec at ages 41-50 years with a standard deviation of 9 percent, the dynamics of arterial state observed in ARS patients correspond to the age-related dynamics of 15-20 years. The V_e/V_m index was 0.78 during the period of disease, 0.87 after two years, and 0.84 after three years. Although the arterial pressure of surviving patients remained normal in the overwhelming majority of cases, the indicator of average hemodynamic pressure increased in parallel with the above-mentioned changes in viscoelastic properties of arteries from 72.2 ± 1.3 mm Hg in the third month after exposure and 76.6 ± 2.1 during the fourth month, to 82.6 ± 1.5 mm Hg three years after exposure.

The quantity and diversity of asthenovegetative disorders is surprising in the recovery period and in the period of immediate consequences in persons surviving ARS following concomitant exposure (first degree ARS) and subclinical forms of radiation injury. Paroxysmic disorders, such as Meniere's disease, diencephalic disorders and vegetative crises, arise in many patients, including ones who had not felt ill in the first two months. For a long time, such persons have extremely low tolerance for hot showers, rough roads, the swaying of a moving vehicle, and various sorts of physical stresses.

Remote stochastic consequences of radiation injury also exhibit a certain dependence upon total absorbed dose of ionizing radiation and its penetrating and highly absorbable (superficial) components [5,28,29]. The opinion has

been suggested that in the case of prolonged low-intensity exposure, the dose-effect ratios are different from those typical of intense short-term exposure in relation to stochastic, nonthreshold effects as well [13,18]. However, that which is undebatable in development of the acute radiation syndrome cannot be extended without sufficient grounds to "single-stroke systems", to nonthreshold—genetic and carcinogenic—effects of radiation exposure.

Thus mutual aggravation of the acute radiation syndrome and of less-than-total radiation burns result in:

1. A disproportion of syndromal manifestations, and an increase in the number of late fatal outcomes among especially severely afflicted patients.
2. Violation of the specific sequence of periods in the course of ARS.
3. Deformation of hematological changes, making biological dosimetry and prediction of the outcome of injury difficult.
4. The ineffectiveness of traditional methods of treating the bone marrow form of ARS, particularly bone marrow transplants.
5. Torpidity of recovery, lengthening of its time.
6. Enrichment of the residual syndrome of radiation sickness.
7. Greater frequency of remote stochastic consequences, especially cancers of superficial location (and possibly hypothyroidism as well, as research on the consequences of the atomic bombings of Hiroshima and Nagasaki showed) [5,28-31].

Bibliography

1. Babayev, N. S., Demin, V. F. and Ilin, L. A., "Yadernaya energetika. Chelovek i okruzhayushchaya sreda" [Nuclear Power Engineering. Man and the Environment], Moscow, 1984.
2. Barabanova, A. V., Baranov, A. Ye. and Guskova, A. K., MED. RADIOL., No 11, 1982, pp 41-44.
3. Baranov, A. Ye., MED. RADIOL., No 8, 1981, p 11.
4. "Radiation Sickness," in "Entsiklopedicheskiy slovar meditsinskiy terminov" [Encyclopedic Dictionary of Medical Terms], Moscow, Vol 1, 1982, p 149.
5. Brilliant, M. D., Vorobyev, A. I. and Gogin, Ye. Ye., TER. ARKH., No 6, 1987, pp 3-8.
6. Brilliant, M. D. and Vorobyev, A. I., PROBL. GEMATOL., No 1, 1972, p 27.
7. Vorobyev, A. I., TER. ARKH., No 12, 1986, pp 3-8.
8. Vorobyev, A. I., Brilliant, M. D., Baranov, A. Ye. et al., KLIN. MED., No 5, 1975, p 69.
9. Gogin, Ye. Ye., TER. ARKH., No 6, 1987, pp 8-14.
10. Gogin, Ye. Ye., VOYEN.-MED. ZHURN., No 4, 1977, pp 32-37.
11. Gogin, Ye. Ye. and Krylov, A. A., "Voyennomorskaya terapiya" [Naval Therapy], Leningrad, 1977, No 8, 200-251.
12. Guskova, A. K., Baranov, A. Ye., Barabanova, A. V. et al., TER. ARKH., No 1, 1989, pp 95-103; No 8, pp 99-103.
13. Guskova, A. K., KLIN. MED., No 2, 1990, pp 6-12.
14. Guskova, A. K. and Baysogolov, G. D., "Luchevaya bolezнь cheloveka" [Radiation Sickness in Man], Moscow, 1971.
15. Zadontsev, V. I., Korsunenkov, L. A., Nikolayev, B. N. and Rykov, M. I., "Dozimetriya radioaktivnykh gazov i aerorozley na sudakh" [Dosimetry of Radioactive Gases and Aerosols Aboard Ship], Leningrad, 1965.
16. Izrael, Yu. A., Petrov, V. A., Pressman, A. Ya. et al., "Radioaktivnoye zagryazneniye prirodnykh sred pri podzemnykh yadernykh vzryvakh i metody yego prognozirovaniya" [Radioactive Contamination of Natural Environments by Underground Nuclear Bursts, and the Methods of Its Prediction], Leningrad, 1970.
17. Ilin, L. A., Arkhangel'skaya, G. V., Konstantinov, Yu. O. and Likhtarev, I. A., "Radioaktivnyy yod v probleme radiatsionnoy bezopasnosti" [Radioactive Iodine in the Problem of Radiation Safety], Moscow, 1972.
18. Ilin, L. A. and Pavlovskiy, O. A., ATOMNAYA ENERGIYA, No 2, 1988, pp 119-129.
19. Kurshakov, N. A., Baysogolov, G. D., Guskova, A. K. et al., MED. RADIOL., No 4, 1966, p 15.
20. Moiseyev, A. A. and Ramzayev, P. V., "Tseziy-137 v biosfere" [Cesium-137 in the Biosphere], Moscow, 1975.
21. Osanov, D. P. and Panova, V. P., "Diagnostika i prognozirovaniye luchevogo porazheniya kozhi" [Diagnosis and Prediction of Radiation Injury to the Skin], Moscow, 1984.
22. Osanov, D. P. and Likhtarev, I. A., "Dozimetriya izlucheniya inkorporirovannykh radioaktivnykh veshchestv" [Dosimetry of Emissions From Incorporated Radioactive Matter], 2d Edition, Moscow, 1977.
23. Barabanova, A. V., Baranov, A. Ye., Guskova, A. K. et al., "Ostryye efekty obлучeniya cheloveka" [Acute Effects of Radiation Exposure in Man], Moscow, 1986.
24. Pyatkin, Ye. K., Filyushkin, I. V. and Nugis, V. Yu., TER. ARKH., No 9, 1986, pp 30-33.

25. Pyatkin, Ye. K. and Baranov, A. Ye., "Biologicheskaya indikatsiya dozy s pomoshchyu analiza aberrantnykh khromosom i kolichstva kletok v perifericheskoy krovi" [Biological Dose Indication by Analysis of Aberrant Chromosomes and the Peripheral Blood Cell Count], Moscow, 1980.

26. Pyatkin, Ye. K., Baranov, A. Ye. and Pokrovskaya, V. N., TER. ARKH., No 8, 1977, p 101.

27. Suvorova, L. A. Vyalova, N. A., Barabanova, A. V. et al., TER. ARKH., No 9, 1981, p 127.

28. Masuyama, M., "Dannyye issledovaniy gruppy Tokyuskogo universiteta" [Data of the Tokyo University Research Group], Hiroshima, 1985.

29. Ito, Ch., "Results of Medical Examinations of A-Bomb Survivors Health Clinic," Hiroshima, 1986.

30. Kurihara, M., Munaka, M., Hayakawa, N. et al., J. RADIAT. RES., Vol 22, 1981, pp 456-471.

31. Oguma, N., Abe, T., Segawa, T. and Kuramoto, A., FUNKT. BIOL. MED., Vol 4 No 1, 1985, pp 1-6.

COPYRIGHT: Izdatelstvo "Meditsina", 1990

Changes in Electrical Parameters of Rat Skin During Radiation

917C0097E Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 24 No 4, Jul-Aug 90 (manuscript received 13 Apr 89) pp 34-36

[Article by S. N. Katasonov, S. K. Shishkina, I. O. Maltseva, and T. Ya. Ryabova]

UDC 612.79.014.423.014.482

[Abstract] The potential for recording the effects of 8.3 and 15 Gr of gamma radiation using electrical parameters of the skin and developing new techniques of biologically predicting radiation exposure was examined on 85 white Wistar female rats (150 - 200 g). The technique was developed to calculate the equivalent electrical resistance of an area of skin and the equivalent electromotive force of the object being measured. The results demonstrated that the electrical parameter of the skin, as measured with the EDFS-10 apparatus, normally varies widely in time. In the animals in the group irradiated with 8.3 Gr for 30 min, skin resistance began on day 2 and peaked on day 7, exceeding figures for the control group by 2.2 - 7.8 fold. The animals in this group also exhibited a second peak in skin resistance 1 - 2 days before death. In animals exposed to a 15 Gr radiation dose, the electrical resistance of the skin peaked at day 3. The results demonstrate that the electrical parameters of the skin undergo significant alterations following gamma radiation exposure. These studies are directed at developing a reliable means of assessing radiation exposure of

biological subjects that is applicable to man, non-invasive, and easy to use, all of which are important to evaluating radiation exposure in space flight. Figures 2; references 5: 3 Russian, 2 Western.

Physiological Aspects of Dogs' Ability to Maintain Posture During Primary Reaction to Radiation

917C0097G Moscow KOSMICHESKAYA BIOLOGIYA I AVIAKOSMICHESKAYA MEDITSINA in Russian Vol 24 No 4, Jul-Aug 90 (manuscript received 25 Nov 88) pp 38-40

[Article by V. N. Malakhovskiy, O. A. Stemparchetskiy, and M. I. Bokk]

UDC 612.76.014.481/.482

[Abstract] Based on the hypothesis that maintaining a vertical pose is a physiological function that makes it possible to record the condition of fine mechanisms of sensorimotor coordination without special animal training, a number of different indices of the stabilograph were studied during the primary reaction to irradiation. Those indices that corresponded to sensorimotor coordination disorders and execution of operations were isolated and tested on male dogs (18 - 20 kg) trained to jump across barriers of increasing height or cross beams of decreasing width. Visual observation prior to irradiation showed that the standing position exhibited the highest degree of muscular tonus. For 30 min following a 10 Gr dose of radiation (1.7 Gr/min) it was difficult to select a moment for stabilograph recording. Restlessness was infrequent and followed by vomiting for 1 - 3 h. The peak of this lower amount of activity was reached 3 - 5 h following irradiation. In the group exposed to 80 Gr (1.7 Gr/min), the initial excitement was short-lived. Vomiting began during irradiation and concluded 1 - 2 h later. Disturbances in motor activity between the two groups varied in degree, with the second group exhibiting cerebral disorders such as ataxia, light tremors, and staggering. There was little difference in sensorimotor coordination between the two groups. The results demonstrated that the area of the passive vector of the stabilograph is not very informative for numerical description of the primary reaction, but may be used in conjunction with other data for revealing mechanisms of disorders. The stabilograph was also modified to include a forced impulse displacement of the animal by turning the standard horizontal platform. In conclusion, the area of the passive vector stabilograph reflects phasic changes in the CNS and in functions of maintaining vertical posture during the primary reaction following high doses of radiation exposure. Another informative index of the degree of radiation exposure is how quickly the animal regains its posture after brief displacement of the support platform. This technique is recommended for animal experiments, as it has been demonstrated to be quite economical and informative. Figures 3; references 10: 7 Russian, 3 Western.

Reciprocal Translocations in Mice in Chernobyl Area

917C01004 Moscow RADIOBIOLOGIYA in Russian
Vol 30 No 4, Jul-Aug 90 pp 441-445

[Article by M. D. Pomerantseva, L. K. Ramaya, B. V. Testov, A. V. Chekhovich, V. A. Shevchenko, A. I. Shaks and N. V. Lobanaya, Institute of General Genetics imeni N. I. Vavilov, USSR Academy of Sciences, Moscow, Institute of Biology, Komi Scientific Center, Ural Department, USSR Academy of Sciences, Syktyvkar, Institute of Biophysics, USSR Ministry of Health, Moscow]

UDC 577.391.621.311.25.004.65

[Abstract] An analysis was conducted on the incidence and type of genetic changes in wild and (CBA x C57Bl)F₁ male mice within a 30 km radius of the Chernobyl nuclear power plant in 1986 - 1988. In the case of the wild mice the estimated exposures ranged from 0.002 to 20 μ Gy/g for external γ -irradiation with a 5- to 10-fold greater β -exposure. The inbred mice were exposed for 5 - 25 days. The results demonstrated an overall low incidence of reciprocal translocations of about one per 100 cells, increasing in a dose-dependent fashion to ca. 1.4 percent in mice subjected to maximum exposure. In the case of 74 males exposed during embryogenesis infertility was noted in five (5.4 percent) that were shown to be heterozygotic for reciprocal translocation. The frequency of reciprocal translocations in these animals ranged from 43 - 61 percent. Tables 1; references 10; 4 Russian, 6 Western.

Partial Sterility of Pine Trees in 1986 and 1987 in Chernobyl Area

917C0100B Moscow RADIOBIOLOGIYA in Russian
Vol 30 No 4, Jul-Aug 90 (manuscript received 2 Jun 89)
pp 450-457

[Article by L. V. Khromova, M. G. Romanovskiy and V. A. Dukharev, Forestry Laboratory, USSR Academy of Sciences, Moscow Oblast]

UDC 577.391.621.311.25.004.65

[Abstract] Female sterility was analyzed in pine trees in the Kiev, Chernigov, Bryansk and Moscow oblasts in 1987 - 1988 to assess the effects of the Chernobyl nuclear power plant accident in 1986. The results revealed that exposures of ca. 4 Gy/yr led to partial female sterility due to diminished viability of ovules and seedbuds. In the most heavily affected regions a 41 - 49 percent reduction in viability was seen in seedbuds resulting from pollination in 1985 and subsequently exposed to the radioactive fallout, as well as in seedbuds resulting from pollination in 1986. Figures 2; tables 3; references 26; 24 Russian, 2 Western.

Spontaneous Motor Activity and Physical Endurance in Rats With Radiation Injuries Treated With Radioprotective Agents

917C0100D Moscow RADIOBIOLOGIYA in Russian
Vol 30 No 4, Jul-Aug 90 (manuscript received 11 Jul 89)
pp 522-523

[Article by T. M. Mamadzhanyov, Scientific Research Institute of Medical Radiology, USSR Academy of Medical Sciences, Obninsk]

UDC 577.391.591.496

[Abstract] Therapeutic evaluation was conducted with cystamine in terms of clinical efficacy and physical endurance of 220 - 250 male Wistar rats with radiation injuries induced by 8 Gy γ -irradiation. The animals were treated i.p. with 90 mg/kg of cystamine 15 min before irradiation. The observations demonstrated that irradiation led to a significant reduction in spontaneous motor activity of the rats. Although cystamine treatment had a positive effect on the clinical course of acute radiation sickness and led to limited recovery of spontaneous motor activity, physical endurance was not improved. The level of physical endurance of the cystamine-treated mice 20 days after irradiation was three-fold lower than that displayed by control mice, with no improvement detectable after an additional 10 days of observation. References 5; Russian.

Book on Blood Chemiluminescence for Estimating Radiation Damage

917C0101B Moscow RADIOBIOLOGIYA in Russian
Vol 30 No 4, Jul-Aug 90 p 529

[Review by A. G. Sverdlov of book "Khemilyuminesentsiya krovi pri raditsionnom vozdeystvii" [Chemiluminescence of Blood in Response to Radiation Exposure] by Ya. I. Serkiz, N. A. Druzhina, A. P. Khrenko, I. O. Pavlenko and I. F. Shlumukova, Kiev, Nauk. dumka, 1989, 173 pages]

[Text] The monograph by Ya. I. Serkiz et al. is the result of many years of research on the role of free-radical oxidation in response to radiation injury of the organism, and on the possibilities of using blood chemiluminescence to characterize and predict the outcome of this injury. While the book is based on the authors' own methods and experimental materials, they are presented in unity with contemporary published data, which makes it possible to present the state of the problem in general. In this case the contribution the author collective makes to the study of this problem is rather significant.

Following a short but clear and complete presentation of ideas on the physical and chemical fundamentals of primary and initial processes of radiation injury (Chapter 1), the authors describe the chemiluminescence phenomenon and its mechanisms, dwelling specially on free-radical oxidation of lipids (Chapter 2). Chapter 3

makes an objective assessment of the possibilities of using the chemiluminescent method in biology, and its prospects and limitations. The description of different devices by which to record chemiluminescence is valuable to experimenters. An original device designed by the authors and a method they proposed for describing kinetic chemiluminescence characteristics is of special interest. The laws governing induced H_2O_2 chemiluminescence of blood plasma established by the authors are examined. Methods of automated analysis of chemilumograms on the basis of a cybernetic model are presented. These materials significantly expand the possibilities of the chemiluminescent method, especially when it is used in blood analysis.

As is demonstrated in the monograph, exposure to radiation elicits characteristic phase oscillations of spontaneous chemiluminescence that differ in rats differing in radiosensitivity (Chapter 4). The method's sensitivity rises significantly when chemiluminescence is induced by an electric current. Individual fluctuations in luminescence intensity are smoothed in this case soon after neutron exposure, however, changes in electrochemiluminescence exhibit a certain correlation with radiosensitivity; they are also different in animals after they are exposed to neutron and gamma-radiation. These observations make it possible to use electrochemiluminescence to distinguish between the effects of different forms of radiation, and to predict the outcome of radiation injury. Attempting to penetrate the essence of processes involved in radiation injury to the organism, the authors interpret the features of chemiluminescence and electrochemiluminescence from the standpoint of regulation theory, and they interpret changes in luminescence as a reflection of the biological system's transition from one level of stability to another.

Induced H_2O_2 -chemiluminescence and analysis of its kinetics in relation to eight parameters provide even more information than electrochemiluminescence. Moreover, such analysis may be carried out with just

microquantities of blood, which provides a possibility for repeating analysis on the same specimens several times, and for observing the dynamics of chemiluminescence. The process is found to be dependent in this case on the exposure dose and on the radiosensitivity of each individual, which makes it possible to evaluate this highly important property in different specimens.

Comparison of changes in chemiluminescence and biochemical indicators reveals a relationship between fluctuations in luminescence and shifts in lipid and microelement metabolism, leading to the conclusion that the intensity of luminescence depends not only on the concentration of oxidation substrates but also on the level of catalysis. The liquid fraction of blood and formed elements (their membranes, hemoglobin in erythrocytes) are found to play differing roles in chemiluminescence. The experience of analyzing the luminescence spectrum is extremely interesting. In particular, it shows that the chemiluminescence of blood serum is the product of not only lipids but also proteins. The spectral characteristics of chemiluminescence of blood and its hemolysate change in response to radiation, which once again correlates with the radiosensitivity of animals. Daily, seasonal and developmental changes in radiosensitivity of rats and chemiluminescence of blood are revealed by considerable amounts of data. In a number of cases correlation, sometimes rather strong, is observed between the same changes, which is viewed as yet another important indication of the relationship between radiation injury and the level of free-radical reactions. The monograph is characterized by a clear theoretical position, an abundance of original methods, and a successfully attained goal of not only deepening certain radiobiological conceptions but also providing practical workers with new methods and facts on their basis.

COPYRIGHT: Izdatel'stvo "Nauka" "Radiobiologiya"
[1990]

**Radioimmunoprecipitation in Laboratory
Diagnosis of AIDS: Optimization and Technical
Assessment**

917C0035C Moscow *ZHURNAL MIKROBIOLOGII,
EPIDEMIOLOGII I IMMUNOLOGII in Russian*
No 6, Jun 90 (manuscript received 1 Sep 89) pp 23-30

[Article by S. Yu. Klyushnik, L. M. Selimova and V. M. Zaydes, Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

UDC 616-092:612.017.1.064]-022.7:578.828.6]-
078.334

[Abstract] Radioimmunoprecipitation (RIP) studies were conducted on a series of HIV-infected cell lines to optimize and test RIP for specificity and sensitivity. RIP was equivalent or exceeded immunoblotting and enzyme immunoassay in sensitivity and specificity and uncovered false negative sera. In addition, RIP methodology was used to demonstrate that HIV-2 glycoproteins formed precipitates only with homologous antisera. However, some anti-HIV-2 antisera precipitated HIV-1 proteins p24 and p55. Figures 5; references 35; 7 Russian, 28 Western

**Enhanced Penetration of Human
Immunodeficiency Virus Into Cells With Helper
Virus**

917C0098B Moscow *VOPROSY VIRUSOLOGII
in Russian Vol 35 No 4, Jul-Aug 90 (manuscript
received 5 May 89) pp 312-314*

[Article by N. K. Sharova and A. G. Bukrinskaya, Virology Institute imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

UDC 578.828.6:578.232].08

[Abstract] Following publication of recent studies whose data favor the hypothesis of fusion of the virus sheath to the plasma membrane of the cell as a means of human immunodeficiency virus (HIV) transmission, as opposed to receptor endocytosis, the combined action of HIV and ultraviolet-inactivated Sendai viruses was tested as a means of enhancing HIV penetration into cells. ³⁵S-methionine-labeled HIV was employed to demonstrate that the Sendai virus increases the number of HIV-associated virus proteins in the cells. The results demonstrated that transmembrane penetration of the virus is accomplished by viral fusion proteins that interact with cell membrane lipids. In addition, the Sendai virus is very active and causes the formation of synaplasts and syncytia following brief contact with sensitive cells. It was also shown that HIV possesses an active fusion protein (gp41) which has a high degree of homology with paramyxovirus proteins. Finally, these findings demonstrate that both the HIV and Sendai viruses penetrate the cell by fusing with the plasma membrane and that using the Sendai virus as a helper virus was a means of greatly

enhancing HIV penetration into the cells. Figures 3, tables 1; references 15; 2 Russian, 13 Western

**Cultivation and Physico-Chemical Properties of
Lassa Virus, Josiah Strain**

917C0098C Moscow *VOPROSY VIRUSOLOGII
in Russian Vol 35 No 4, Jul-Aug 90 (manuscript
received 30 May 89) pp 326-329*

[Article by E. M. Fidarov, L. Ye. Surikova, N. I. Yefofeyeva, L. M. Klimashevskaya, A. S. Petkevich, and I. S. Lukashevich, Belorussian Epidemiology and Microbiology Scientific Research Institute, Belorussian SSR Ministry of Health, Minsk]

UDC 578.833.26.083.22

[Abstract] In connection with the prevalence of Lassa virus in the countries of Western Africa and its relatively high mortality rate, effective means of its diagnosis, treatment, and prevention are being sought. Lassa virus affects 200,000 - 300,000 people annually, resulting in 5,000 deaths. The sensitivity of Lassa virus, which as an arenavirus is sensitive to changes in pH and temperature, as well as some salt ions, was investigated using the Josiah strain. Of the five cell lines employed to assess the reproductive activity of the Josiah strain, four (Vero, VNK-21, 4647, and guenon kidney cells) exhibited satisfactory permissiveness. The results demonstrated that the Josiah strain was relatively stable to heat (50°C, 90 min), but could be completely inactivated by urea (1 - 3 M, 15 - 20 min) and formalin (0.03 - 0.2 percent, 24 - 48 h). In addition, ultraviolet light irradiation (10 sec) was also effective in inactivating the Josiah strain. Finally, the results must be considered in the development and manufacture of diagnostic and therapeutic preparations for Lassa fever. Figures 4; tables 2; references 13; 4 Russian, 9 Western

**Comparative Analysis of Hepatitis That is Neither
A nor B With Fecal-Oral Means of Transmission
in USSR and India**

917C0098D Moscow *VOPROSY VIRUSOLOGII
in Russian Vol 35 No 4, Jul-Aug 90 (manuscript
received 12 May 89) pp 342-344*

[Article by I. V. Shakhgildyan, M. S. Chadkha, M. O. Favorov, V. A. Arankalle, P. A. Khukhlovich, A. Sekhgal, T. I. Yashina, S. I. Ramamurti, and G. K. Zairov, Virology Institute imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow; National Virology Institute, Puna, India]

UDC 616.36-002-022.7:578.891]-022.363.3-
036.22[(47+57)+(540)

[Abstract] The results of intensive comparative studies on recent outbreaks (1984 - 1985) of fecal-oral hepatitis that is neither A nor B (HnAnB) in the USSR and India were analyzed with the intent of determining the source

of the disease. Virologic and serologic investigations showed that this peculiar type of viral hepatitis was etiologically distinct from hepatitis viruses A and B which are characterized by fecal-oral means of transmission and from HnAnB with a parenteral means of transmission. The data showed that the disease peaked in October in Turkmenia, while it peaked in March through May in India, the hottest months of the year in these regions. In fecal specimens collected from patients in Turkmenia, immunoelectron microscopy revealed spherical, virus-like particles 27 - 30 nm in diameter. The primary areas affected by this disease, Northern Turkmenia in the USSR and the cities of Surat and Akhmedabad in India, all reported an explosive nature of transmission of the infection which afflicted large numbers of susceptible people in a rather short period of time. Another important distinguishing aspect of HnAnB in these areas was the peculiar age structure of the patients, most of which were aged 15 - 29 years. Moreover, antiviral hepatitis A IgM (a specific marker of acute hepatitis A) was found in only 3 - 4.3 percent of cases, and only in children under the age of three years. Another substantial aspect of the infection was the heterogeneity of the territorial spread of the disease: some residential areas had an incidence of the disease several times higher than that of adjacent areas. Also of concern was the high mortality rate (7.7 - 16.5 percent) among pregnant women, especially those in the second trimester of the pregnancy. All of the data collected indicated that the infections were associated with unsanitary water obtained from wells and open reservoirs for drinking and other domestic purposes. The virologic and serologic data also demonstrated that the etiological agents causing this infection in the USSR and India were identical. References 12: 6 Russian, 6 Western.

Vaccinia Virus Stimulation of Oncogenesis in C57B1 Mice

917C0098 Moscow VOPROSY VIRUSOLOGII in Russian Vol 35 No 4, Jul-Aug 90 (manuscript received 4 Aug 89) pp 344-346

[Article by N. A. Kharkovskaya, S. A. Khrustalev, and Z. I. Merekalova, All-Union Oncological Scientific Center, USSR Academy of Medical Sciences, Moscow]

UDC 616-006-02:615.371:578.821.5]-092.9-07

[Abstract] Data are presented on the development of spontaneous neoplasms and leukemias induced by Rauscher's virus in C57B1/6JY mice, which until recently were thought to be resistant to spontaneous and some induced tumors. These mice were also vaccinated with dry vaccinia virus. Three series of experiments demonstrated that the mice were administered both the vaccinia virus and Rauscher's leukemia virus were much more susceptible to tumor development. Vaccinia virus vaccination was shown to affect not only the frequency of hemoblastoses, but also their severity. Included in the

research were studies on ascorbic acid, which was demonstrated to inhibit the stimulating effect of vaccinia virus vaccination on spontaneous blastomagenesis in the mice. These findings suggest that the vaccinia virus's tendency to increase the number of malignant tumors needs to be considered in the development of recombinant vaccines in which the vaccinia virus vaccine is combined with the genome of other viruses. Tables 1; references 12: 9 Russian, 3 Western.

HIV-Like Particle in Subjects With Indeterminate Immunoblotting Patterns

917C0099A Moscow IMMUNOLOGIYA in Russian No 4, Jul-Aug 90 (manuscript received 12 Jan 90) pp 21-23

[Article by R. M. Khaitov, G. N. Chuvirov, L. P. Trubcheninova, B. V. Pinegin, N. A. Khabakhpacheva, M. Ye. Ishchenko, M. V. Glushchenko, L. S. Yakovleva, Ye. V. Yefremova and S. A. Makarova, Institute of Immunology, USSR Ministry of Health, Moscow]

UDC 616.153.962.4-097-078.33

[Abstract] Examination of 65,911 serum samples between 1985 - 1989 revealed 61 samples with indeterminate immunoenzyme and immunoblotting results. Electron microscopic studies on the plasma of two of the latter subjects at six month intervals for 1.5 years revealed typical, 110 - 140 nm, HIV-like particles. Most frequently the sera of these subjects were positive for antibodies against the p24 protein in immunoblotting studies. Control studies on sera routinely showing high titer in immunoenzyme studies and positive on immunoblotting regularly yielded the virus-like particles observed in the cases of dubious immunoblotting results. Figures 2; tables 1; references 9: 1 Russian, 8 Western.

In Vitro Protective Action of Antisera Against Synthetic Fragment of HIV-1 gag Gene Protein p24

917C0099B Moscow IMMUNOLOGIYA in Russian No 4, Jul-Aug 90 (manuscript received 28 May 89) pp 23-25

[Article by A. L. Liozner, A. N. Byzina, M. N. Korneyeva, S. M. Andreyev, L. B. Kalnina and M. G. Vafina, Institute of Immunology, USSR Ministry of Health; Institute of Virology imeni D. I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow]

UDC 616.98:578.828.6]-092:612.017.1]-078.3

[Abstract] Antisera were generated in rabbits against the 219 - 229 amino acid sequence of the core antigen (p24) of HIV-1, employing a synthetic peptide conjugated to a high MW carrier as the immunogen. Subsequent studies showed that the anti-peptide sera protected lymphoblastoid MT-4 cells in tissue culture against infection with HKTIV-IIIRF virus. The results constitute the first demonstration that antibodies against the HIV-1 core antigen can protect lymphoid cells from invasion by HTLV. Figures 1; references 12: 2 Russian, 10 Western.

Detection of HIV Antibodies by Agglutination of Latex Particles Coated With Synthetic Epitopes

917C0099C Moscow IMMUNOLOGIYA in Russian
No 4, Jul-Aug 90 (manuscript received 27 Mar 89)
pp 29-30

[Article by I. G. Sidorovich, S. P. Pavlikov, I. A. Nikolayeva, L. Yu. Sklyarov, V. S. Ivanov, L. D. Chikin, A. T. Kozhich, O. A. Kaurov, A. N. Prusakov and S. B. Ulyanchenko, Institute of Immunology, USSR Ministry of Health; Institute of Bioorganic Chemistry imeni M. M. Shemyakin, USSR Academy of Sciences, Moscow; All-Union Scientific Research Institutes of Highly Purified Biological Preparations (Leningrad) and of Biological Instrumentation (Moscow), USSR Ministry of Medical Industry]

UDC 616.98:578.828.6]-092:612.017.1.064]-
07:616.153.96-097-078.33

[Abstract] Latex agglutination tests were conducted on sera obtained from 50 patients with HIV-1 and two patients with HIV-2, employing synthetic peptides for coating the particles. The peptide fragments corresponded to the C-terminal end of gp120 of HIV-1, and the N-terminal ends of gp41 of HIV-1 and gp36 of HIV-2. The system was found to yield positive results in each case and was equivalent to solid-phase immunoenzyme assays in sensitivity. In addition, the results of the latex agglutination tests were not affected by heating the sera at 56°C for 30 min, although such treatment has been reported to affect the results of immunoenzyme assays. Tables 3; references 6: 1 Russian, 5 Western.

Computerized Surveillance of Antimicrobial Resistance of Pyogenic Pathogens

917C0140A Moscow ANTIBIOTIKI I

KHIMIOTERAPIYA in Russian Vol 35 No 10, Oct 90
(manuscript received 12 Mar 90) pp 19-20

[Article by N. A. Semina, K. K. Gladkova, D. L. Vinograd, I. V. Pavlenishvili, P. Urbashkova, P. Petrash, G. A. Kotlyarova, Ye. M. Kondratyeva, N. V. Makarova and N. V. Umrikhina, Central Scientific Research Institute of Epidemiology, USSR Ministry of Health, Moscow]

UDC 616.94+616-002.3-022.7:[579.252.55:616.33]-078:681.31

[Abstract] Multi-center study was conducted on computerized surveillance of antibiotic resistance of pyogenic bacteria isolated from obstetrical, burn, and infectious disease patients. Differences among the various cities (Omsk, Minsk, Smolensk, Samarkand, Tbilisi, Vilnyus) were found to be insignificant. However, in close to 7 percent of the isolates disparate results were obtained by disk-diffusion and the computerized MS-2 system (USA). Furthermore, moderate discrepancies were noted with almost 60 percent of the isolates. In addition, some 90 percent of the isolates displayed multiple resistance. The information was used to construct a data bank for use in delineating effective antibiotic therapy strategies. References 8: 3 Russian, 5 Western.

Cloning of aacC2 Gene From E.coli Clinical Isolate

917C0140C Moscow ANTIBIOTIKI I

KHIMIOTERAPIYA in Russian Vol 35 No 10, Oct 90
(manuscript received 12 Feb 90) pp 43-45

[Article by Ye. G. Entina and S. B. Vakulenko, All-Union Scientific Research Institute of antibiotics, Moscow]

UDC 579.842.11:579.252.55

[Abstract] The replicon dissociation technique [Entina, Ye. G., Preparation, Investigation and Application of Antibiotics and BAV [sic] (in Russ.), Moscow, 1990, pp 18-19] was employed in cloning the aacC2 gene (encoding aminoglycoside acetyltransferase AAC(3)-II) of a clinical isolate of *E. coli*. The methodology utilized vector plasmids pUC18 and pUC19, a 2.3 kb DNA fragment prepared with HindIII and transformation of *E. coli* JM101. In the final analysis a low MW plasmid was obtained which, on further restriction analysis, was shown to bear the aacC2 gene in a 1.1 kb fragment prepared with Sall and Alul restriction enzymes. Figures 1; tables 1; references 22: 9 Russian, 13 Western.

Nucleotide Sequence of Gene aacC2 of E. coli Clinical Isolate

917C0140D Moscow ANTIBIOTIKI I

KHIMIOTERAPIYA in Russian Vol 35 No 10, Oct 90
(manuscript received 12 Feb 90) pp 46-50

[Article by S. B. Vakulenko and Ye. G. Entina, All-Union Scientific Research Institute of antibiotics, Moscow]

UDC 579.842.11:579.252.55

[Abstract] Sequencing studies were conducted on gene aacC2, responsible for gentamicin resistance by encoding aminoglycoside acetyltransferase (AAC(3)-II), derived from a clinical isolate of *E. coli*. aacC2 was represented in a 2273 bp HindIII fragment incorporated into plasmid pSV11. Computerized analysis of the sequencing results demonstrated that the aacC2 gene was contained in a 858 bp fragment positioned in the 819-1676 nucleotide sequence (beginning at the 5'-end), and encoded a 286 amino acid 30.6 kD protein. Sequence comparison revealed that the gene cloned in pSV11 contained 5 percent nucleotide substitutions vis-a-vis aacC2 identified in plasmids pWP14a, pWP116a, pJV03 abd pWP113a, accounting for 7.3 percent amino acid substitutions in the protein product. Figures 5; references 7: 2 Russian, 5 Western.

END OF

FICHE

DATE FILMED

30 April 1991